

Strategies to Prevent or Remediate Cancer and Treatment-Associated Aging Annotated Bibliography

Table of Contents

Annotated Bibliography Methods	2
Physical Activity Interventions.....	5
Original Research	5
Physical Activity Interventions.....	14
Reviews.....	14
Nutrition Interventions	20
Original Research	20
Nutrition Interventions	21
Reviews.....	21
Multicomponent Interventions	23
Original Research	23
Multicomponent Interventions	34
Reviews.....	34
Cognitive Interventions.....	37
Original Research	37
Cognitive Interventions.....	44
Reviews.....	44
Supportive Care Interventions.....	46
Original Research	46
Supportive Care Interventions.....	55
Reviews.....	55
Other types of interventions.....	60
Original Research	60
Other types of interventions.....	61
Reviews.....	61

Annotated Bibliography Methods

We conducted a rapid review to provide a broad overview of the body of evidence on interventions and strategies to prevent or mitigate accelerating aging in cancer survivors; particularly interventions aiming to reduce long term effects of cancer and cancer treatment.

The purpose of the rapid review was to inform discussions at the “Strategies to Prevent or Remediate Cancer and Treatment-Associated Aging” Think Tank Meeting hosted by NCI on February 11-12, 2019.

A rapid review is “a type of knowledge synthesis in which components of the systematic review process are simplified or omitted to produce information in a short period of time”.¹ A rapid review provides a broad overview of a topic and can inform additional methods to gather evidence, including systematic reviews. The section below outlines the specific steps followed for this rapid review:

1. Developed and tested search terms (key words) to be used in primary searches: Different sets of key words were tested in searches including:

- (Interventions AND cancer AND accelerated aging)
- (Interventions AND cancer treatment AND premature aging)
- (Interventions AND cancer treatment AND aging outcomes)
- (Interventions AND cancer survivors)

2. Conducted primary searches using three sets of key terms in the PubMed data base

- (Interventions AND cancer AND accelerated aging)
- (Interventions AND cancer treatment AND premature aging)
- (Interventions AND cancer treatment AND aging outcomes)

3. Conducted triage of primary search results:

Titles and abstracts were screened to identify eligible studies. Full text articles were screened when the abstract did not provide enough information for inclusion. A formal triage process documenting excluded

¹ Trico AC, Antony J, Zarin W, et al. A scoping review of rapid review methods. *BMC Med.* 2015;13:224. Published 2015 Sep 16. doi:10.1186/s12916-015-0465-6

sources was not conducted for the purpose of the rapid review. Eligibility was assessed using the following inclusion criteria:

- Peer reviewed articles (systematic reviews or original research) published between 2009 and 2019
- Interventions to mitigate or prevent age-related consequences of cancer and cancer treatment, particularly of systematic cancer treatment and radiation including:
 - Physical activity
 - Nutrition
 - Multicomponent
 - Supportive care
 - Cognitive
- Interventions conducted among adult populations
- Any age-related outcome of cancer or cancer treatment
- Articles reporting only on health-related quality of life (HRQoL) or weight/BMI outcomes were excluded

4. Conducted supplementary targeted searches:

Targeted searches were conducted to supplement the articles identified through the primary searches and to ensure that there were relevant articles that addressed all the types of interventions that will be discussed during the second day of the Think Tank. For example, the primary searches identified numerous papers about physical activity interventions so more targeted searches were conducted on cognitive interventions. Targeted searches were conducted using the “similar articles” feature from PubMed. PubMed uses a word-weighted algorithm to compare words from the title and abstract of each citation and the assigned MeSH headings. The similar articles feature was applied to both relevant articles identified through the primary searches and the targeted searches.

5. Summarized all relevant papers using an annotated bibliography template that included: full reference, abstract, type of intervention, description of the intervention, outcomes, summary of main points, and research gaps.

Physical Activity Interventions

Original Research

Cormie, P, Galvao, DA, Spry, N, et al. (2015). Can supervised exercise prevent treatment toxicity in patients with prostate cancer initiating androgen-deprivation therapy: a randomised controlled trial. BJU international 115: 256-266.

Abstract: OBJECTIVE: To determine if supervised exercise minimises treatment toxicity in patients with prostate cancer initiating androgen-deprivation therapy (ADT). This is the first study to date that has investigated the potential role of exercise in preventing ADT toxicity rather than recovering from established toxicities. PATIENTS AND METHODS: Sixty-three men scheduled to receive ADT were randomly assigned to a 3-month supervised exercise programme involving aerobic and resistance exercise sessions commenced within 10 days of their first ADT injection (32 men) or usual care (31 men). The primary outcome was body composition (lean and fat mass). Other study outcomes included bone mineral density, physical function, blood biomarkers of chronic disease risk and bone turnover, general and prostate cancer-specific quality of life, fatigue and psychological distress. Outcomes were compared between groups using analysis of covariance adjusted for baseline values. RESULTS: Compared to usual care, a 3-month exercise programme preserved appendicular lean mass ($P = 0.019$) and prevented gains in whole body fat mass, trunk fat mass and percentage fat with group differences of -1.4 kg ($P = 0.001$), -0.9 kg ($P = 0.008$) and -1.3% ($P < 0.001$), respectively. Significant between-group differences were also seen favouring the exercise group for cardiovascular fitness (peak oxygen consumption 1.1 mL/kg/min, $P = 0.004$), muscular strength (4.0 - 25.9 kg, $P \leq 0.026$), lower body function (-1.1 s, $P < 0.001$), total cholesterol: high-density lipoprotein-cholesterol ratio (-0.52 , $P = 0.028$), sexual function (15.2 , $P = 0.028$), fatigue (3.1 , $P = 0.042$), psychological distress (-2.2 , $P = 0.045$), social functioning (3.8 , $P = 0.015$) and mental health (3.6 - 3.8 , $P \leq 0.022$). There were no significant group differences for any other outcomes. CONCLUSION: Commencing a supervised exercise programme involving aerobic and resistance exercise when initiating ADT significantly reduced treatment toxicity, while improving social functioning and mental health. Concurrent prescription of supervised exercise when initiating ADT is therefore advised to minimise morbidity associated with severe hypogonadism.

Publication Year: 2015	Addresses Premature Aging Specifically: No
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Target Population: 63 men, with prostate cancer scheduled to initiate androgen-deprivation therapy (ADT)	Type of Intervention: Physical Activity
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Description of Intervention: Exercise training: Two-armed prospective randomized controlled trial design. After familiarization and baseline testing sessions, participants were randomized into the two arms:

- Exercise: 60-minutes group-based sessions, 2x/week for 3 months, supervised by accredited exercise physiologists. Sessions included:
 - 20-30 minute of moderate–high intensity aerobic exercise (e.g., treadmill, cycling, rowing)
 - Resistance exercises (e.g., upper and lower body weight exercises)
 - Standard warm-up and cool-down periods
- Usual care

Long Term Cancer Effect Addressed:

- Body composition: lean and fat mass
- Physical function: series of standard tests (e.g., 400-m walk test, maximal strength of the lower and upper body, chair rise and stair climb tests, 6-m walk)
- Bone mineral density: Areal BMD (g/cm²) hip (femoral neck), lumbar spine (L2–4) and whole assessed by DXA
- Other outcomes: blood biomarkers of chronic disease risk and bone turnover, general and prostate cancer-specific quality of life, fatigue and psychological distress

Summary of Main Points:

- Commencing a supervised exercise program when initiating ADT significantly reduced the severity of adverse side-effects
- Body composition: appendicular lean mass was essentially preserved in the exercisers compared with the usual-care group, who lost ≈ 0.6 kg, while fat mass, trunk fat mass and percentage fat increased with usual care and decreased in the exercise group. Additionally, exercise mitigated the loss in whole body lean mass
- Physical function: compared to the usual-care group, the exercise group significantly improved in cardiovascular fitness, maximal strength and lower body function (repeated chair rise)

- Improvements in the exercise group were also observed for total cholesterol: HDL-cholesterol ratio, sexual function, fatigue and psychological distress
- Bone Mineral Density: The exercise programmed did not attenuate the decline in BMD seen over the initial 3-month period of ADT. Potential reasons include short duration of the study and not inclusion of specific bone targeting high impact exercises
- There were also clinically significant improvements in social functioning and mental health after the 3-month exercise program

Research Gaps: •The short-term nature of the intervention may have precluded the ability to observe changes in bone outcomes and markers of chronic disease risk. Future trials involving longer intervention and incorporation of follow-up periods are warranted

- Improvements in physical strength and fitness, particularly in the context of group peer support, may directly address masculine self-esteem and may also be more acceptable to men than traditional support models that are accessed less by men than women. This is a critical area for future research

Dawson, JK, Dorff, TB, Todd Schroeder, E, et al. (2018). Impact of resistance training on body composition and metabolic syndrome variables during androgen deprivation therapy for prostate cancer: a pilot randomized controlled trial. BMC cancer 18: 368.

Abstract: BACKGROUND: Prostate cancer patients on androgen deprivation therapy (ADT) experience adverse effects such as lean mass loss, known as sarcopenia, fat gain, and changes in cardiometabolic factors that increase risk of metabolic syndrome (MetS). Resistance training can increase lean mass, reduce body fat, and improve physical function and quality of life, but no exercise interventions in prostate cancer patients on ADT have concomitantly improved body composition and MetS. This pilot trial investigated 12 weeks of resistance training on body composition and MetS changes in prostate cancer patients on ADT. An exploratory aim examined if a combined approach of training and protein supplementation would elicit greater changes in body composition. METHODS: Prostate cancer patients on ADT were randomized to resistance training and protein supplementation (TRAINPRO), resistance training (TRAIN), protein supplementation (PRO), or control stretching (STRETCH). Exercise groups (EXE = TRAINPRO, TRAIN) performed supervised exercise 3 days per week for 12 weeks, while non-exercise groups (NoEXE = PRO, STRETCH) performed a home-based stretching program. TRAINPRO and PRO received 50 g/day (-1) of whey protein. The primary outcome was change in lean mass assessed through dual energy x-ray absorptiometry. Secondary outcomes examined changes in sarcopenia, assessed through appendicular skeletal mass (ASM) index (kg/m²), body fat %, strength, physical function, quality of life, MetS score and the MetS components of waist circumference, blood pressure, glucose, high-density lipoprotein-cholesterol, and triglyceride levels. RESULTS: A total of 37 participants were randomized; 32 participated in the intervention (EXE n = 13; NoEXE n = 19). At baseline, 43.8% of participants were sarcopenic and 40.6% met the criteria for MetS. Post-intervention, EXE significantly improved lean mass (d = 0.9), sarcopenia prevalence (d = 0.8), body fat % (d = 1.1), strength (d = 0.8-3.0), and prostate cancer-specific quality of life (d = 0.9) compared to NoEXE (p < 0.05). No significant differences were observed between groups for physical function or MetS-related variables except waist circumference (d = 0.8). CONCLUSIONS: A 12-week resistance training intervention effectively improved sarcopenia, body fat %, strength and quality of life in hypogonadal prostate cancer patients, but did not change MetS or physical function. PRO did not offer additional benefit in improving body composition.

Publication Year: 2018

Addresses Premature Aging Specifically: No

Target Population: 37 prostate cancer patients on ADT

Type of Intervention: Physical Activity

Description of Intervention: Resistance training program: patients randomized to exercise, one of two resistance training interventions (TRAINPRO and TRAIN), or controls (stretching)

- TRAINPRO AND TRAIN groups: resistance training: ~ 50 min/session; 3 days/week; 12 weeks with an accredited exercise trainer at Clinical Exercise Research Center
- Each session began with a 5 min warmup. The training routine included 7 machine-based exercises and 3 trunk exercises
- Alternative exercises offered to metastatic patients (body weight exercises, and resistance bands)
- TRAINPRO was also given 50 g·day⁻¹ of whey protein isolate

Long Term Cancer Effect Addressed: • Sarcopenia: appendicular skeletal mass index (DXA)

- Body composition: lean mass, fat free mass, fat mass and body fat % following a 12-h fast (DXA)
- Physical function: 400 m walk, the timed up and go, and a stair climb
- Other outcomes: Metabolic syndrome, QoL, muscle strength

Summary of Main Points: • After 12 weeks, the exercise group significantly attenuated sarcopenia prevalence compared to the NoEXE group

- Post-intervention, the exercise group significantly increased muscle mass (lean mass) and decreased body fat %
- Functional outcomes: strength improved (significant), the other functional outcomes improved (not significant)
- This study demonstrated that 12 weeks of vigorous-intensity resistance training could counter treatment-related sarcopenia and fat gain, increase upper and lower extremity strength, and enhance prostate cancer-specific quality of life in prostate cancer patients on ADT

Research Gaps: • Future investigations wishing to employ higher doses of protein intake may need to consider subtle effects of long-term supplementation on kidney function or other complicating factors

Galvao, DA, Spry, N, Denham, J, et al. (2014). A multicentre year-long randomised controlled trial of exercise training targeting physical functioning in men with prostate cancer previously treated with androgen suppression and radiation from TROG 03.04 RADAR. European urology 65: 856-864.

Abstract: BACKGROUND: Long-term prostate cancer (PCa) survivors are at increased risk for comorbidities and physical deconditioning. OBJECTIVE: To determine the effectiveness of a year-long randomised controlled trial of exercise training in PCa survivors >5 yr postdiagnosis on physical functioning. DESIGN, SETTING, AND PARTICIPANTS: Between 2010 and 2011, 100 long-term PCa survivors from Trans-Tasman Radiation Oncology Group 03.04 Randomised Androgen Deprivation and Radiotherapy previously treated with androgen-deprivation therapy and radiation therapy were randomly assigned to 6 mo of supervised exercise followed by 6 mo of a home-based maintenance programme (n=50) or printed educational material about physical activity (n=50) for 12 mo across 13 university-affiliated exercise clinics in Australia and New Zealand. INTERVENTION: Supervised resistance and aerobic exercise or printed educational material about physical activity. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: The primary end point was a 400-m walk as a measure of cardiovascular fitness. Secondary end points were physical function, patient-reported outcomes, muscle strength, body composition, and biomarkers. Analysis of covariance was used to compare outcomes for groups at 6 and 12 mo adjusted for baseline values. RESULTS AND LIMITATIONS: Participants undergoing supervised exercise showed improvement in cardiorespiratory fitness performance at 6 mo (-19 s [p=0.029]) and 12 mo (-13 s [p=0.028]) and better lower-body physical function across the 12-mo period (p<0.01). Supervised exercise also improved self-reported physical functioning at 6 (p=.006) and 12 mo (p=0.002), appendicular skeletal muscle at 6 mo (p=0.019), and objective measures of muscle strength at 6 and 12 mo (p<0.050). Limitations included the restricted number of participants undertaking body composition assessment, no blinding to group assignment for physical functioning measures, and inclusion of well-functioning individuals. CONCLUSIONS: Supervised exercise training in long-term PCa survivors is more effective than physical activity educational material for increasing cardiorespiratory fitness, physical function, muscle strength, and self-reported physical functioning at 6 mo. Importantly, these benefits were maintained in the long term with a home-based programme with follow-up at 12 mo. CLINICAL TRIAL REGISTRY: The effect of an exercise intervention on cardiovascular and metabolic risk factors in prostate cancer patients from the RADAR study, ACTRN: ACTRN12609000729224.

Publication Year: 2014	Addresses Premature Aging Specifically: No
Target Population: 100 long-term prostate cancer survivors previously treated with androgen-deprivation therapy and radiation therapy	Type of Intervention: Physical Activity
Description of Intervention: Supervised exercise: patients were randomly assigned to 6 months of supervised resistance and aerobic exercise followed by 6 months of a home-based maintenance program OR printed educational material about physical activity	
Long Term Cancer Effect Addressed: <ul style="list-style-type: none"> •Physical Function: lower-body physical function and self-reported •Body composition: appendicular skeletal muscle •Other outcomes: cardiovascular fitness (400-m walk), patient-reported outcomes, muscle strength 	
Summary of Main Points: <ul style="list-style-type: none"> •Supervised exercise training in long-term PCa survivors is more effective than physical activity educational material for increasing cardiorespiratory fitness, physical function, muscle strength, and self-reported physical functioning at 6 mo •These benefits were maintained in the long term with a home-based program with follow-up at 12 mo 	
Research Gaps: None reported by authors	

Irwin, ML, Cartmel, B, Harrigan, M, et al. (2017). Effect of the LIVESTRONG at the YMCA exercise program on physical activity, fitness, quality of life, and fatigue in cancer survivors. Cancer 123: 1249-1258.

Abstract: BACKGROUND: Physical activity (PA) has been linked to a lower risk of developing and dying of cancer, yet many cancer survivors do not exercise. In the current study, the authors evaluated the impact of the LIVESTRONG at the YMCA exercise program, available at Young Men's Christian Associations (YMCAs) across the United States, on PA, fitness, quality of life, fatigue, body composition, serum biomarkers, and program safety in cancer survivors. METHODS: Cancer survivors were recruited through the Yale Cancer Center and the Dana-Farber Cancer Institute and randomized to a 12-week, twice-weekly LIVESTRONG at the YMCA exercise program at YMCAs in Connecticut or Massachusetts or to a control group. Questionnaires, dual-energy x-ray absorptiometry scans, 6-minute walk tests (6MWTs), and a fasting blood draw were completed at baseline and at 12 weeks. Intervention effects were evaluated using mixed model repeated measures analysis, with changes at 12 weeks in PA and 6MWT as the primary endpoints. RESULTS: A total of 186 participants were randomized (95 to the exercise group and 91 to the control group). The majority of patients were diagnosed with AJCC stage I to II cancer and 53% had breast cancer. Participants randomized to the LIVESTRONG at the YMCA program experienced increases in PA (71% exercising at ≥ 150 minutes/week vs 26% of controls; $P < .05$) and improvements in the 6MWT (group difference: 28.9 meters [95% confidence interval, 0.3-49.0; $P = .004$]) and quality of life (group difference: 2.6 [95% confidence interval, 0.1-5.0; $P = .04$]). No adverse events were reported. CONCLUSIONS: The LIVESTRONG at the YMCA exercise program has the potential to impact thousands of survivors across the YMCA network and could lead to improvements in disease and psychosocial outcomes in the growing population of cancer survivors. Cancer 2017;123:1249-1258. (c) 2016 American Cancer Society.

Publication Year: 2017

Addresses Premature Aging Specifically: No

Target Population: Cancer survivors

Type of Intervention: Physical Activity

Description of Intervention: Structured exercise:

- LIVESTRONG at the YMCA exercise program: sessions led by two YMCA fitness instructors; aerobic exercise, resistance training exercises
- 90-minutes sessions/2 X week
- 12-weeks intervention

Long Term Cancer Effect Addressed: •Physical Function/Cardiorespiratory Fitness: Six Minute Walk Test (6MWT)

- Body composition: DEXA scans were performed to assess body fat, lean body mass (LBM) and total bone mineral density (BMD)
- Other outcomes: Blood Draw and Serum Biomarkers, Quality of Life and Fatigue, Safety Evaluation/Injury Questionnaire, physical activity (PA) behavior

Summary of Main Points: •The LIVESTRONG at the YMCA program was effective in improving PA, fitness/function (6MWT), QOL and cancer-related fatigue in a mixed group of cancer patients, including long-term cancer survivors, newly-diagnosed patients receiving adjuvant therapy, and individuals living with advanced disease. Benefits were seen both in patients who were more and less active at baseline

- There was no effect of the LIVESTRONG at the YMCA exercise program on body composition or serum biomarkers. This study enrolled both physically active and inactive participants, with a range of BMI levels and different cancer types, which may confound the ability to determine an effect of exercise on body composition, insulin and CRP
- These findings provide important data regarding the physical and psychological benefits, as well as the safety, of the LIVESTRONG at the YMCA exercise program in cancer survivors, and may support the continued implementation of the LIVESTRONG at the YMCA program in YMCA facilities across the country

Research Gaps: •Future studies are needed to evaluate the dose-response effect of the LIVESTRONG at the YMCA program and whether additional sessions per week or higher intensity of exercise is necessary

- Additional studies evaluating maintenance of physical activity over time, and to how to improve attendance to the exercise sessions and associated predictors of attendance
- It is important to examine the effectiveness of the LIVESTRONG at the YMCA exercise program by geography, race/ethnicity and socio-economic status

Saarto, T, Sievanen, H, Kellokumpu-Lehtinen, P, et al. (2012). Effect of supervised and home exercise training on bone mineral density among breast cancer patients. A 12-month randomised controlled trial. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 23: 1601-1612.

Abstract: The ability of combined step aerobic- and circuit-training to prevent bone loss after breast cancer treatments was related to skeletal site and patients' menopausal status. Among premenopausal breast cancer survivors, a 12-month exercise intervention completely prevented bone loss at the femoral neck, whereas no exercise effect was seen at lumbar spine or at neither site in postmenopausal women. **INTRODUCTION:** The primary objective of this randomised clinical trial was to determine the preventive effect of supervised weight-bearing jumping exercises and circuit training on bone loss among breast cancer patients. **METHODS:** Of 573 breast cancer survivors aged 35-68 years randomly allocated into exercise or control group after adjuvant treatments, 498 (87%) were included in the final analysis. The 12-month exercise intervention comprised weekly supervised step aerobic- and circuit-exercises and similar home training. Bone mineral density (BMD) at lumbar spine and femoral neck were measured by dual-energy X-ray absorptiometry. Physical performance was assessed by 2-km walking and figure-8 running tests, and the amount of physical activity was estimated in metabolic equivalent-hours/week. **RESULTS:** In premenopausal women, bone loss at the femoral neck was prevented by exercise, the mean BMD changes being -0.2% among the trainees vs. -1.4% among the controls ($p = 0.01$). Lumbar bone loss could not be prevented (-1.9% vs. -2.2%). In postmenopausal women, no significant exercise-effect on BMD was found either at the lumbar spine (-1.6% vs. -2.1%) or femoral neck (-1.1% vs. -1.1%). **CONCLUSIONS:** This 12-month aerobic jumping and circuit training intervention completely prevented femoral neck bone loss in premenopausal breast cancer patients, whereas no effect on BMD was seen in postmenopausal women.

Publication Year: 2012	Addresses Premature Aging Specifically: No
Target Population: Breast cancer survivors after completion of their adjuvant chemotherapy and postoperative radiotherapy	Type of Intervention: Physical Activity
<p>Description of Intervention: Supervised weight-bearing aerobic jumping and circuit exercises complemented by similar home training:</p> <ul style="list-style-type: none"> •12-month intervention •The weekly training program comprised one supervised session of vigorous step aerobics or circuit training and two to three similar home training sessions •Supervised training sessions were organized in the small groups of five to 15 subjects and were led by experienced physical therapists •Home training consisted mainly of endurance training such as walking, Nordic walking or aerobic training, and also osteogenic elements, also about 100 similar leaps and jumps per training session as were used in the circuit training sessions 	
<p>Long Term Cancer Effect Addressed:</p> <ul style="list-style-type: none"> •Bone mineral density (BMD)/bone loss: lumbar spine and femoral neck were measured by DXA •Co-morbidities: •Cancer recurrence •All-cause mortality •QoL, cardiorespiratory fitness, health economy 	
<p>Summary of Main Points:</p> <ul style="list-style-type: none"> •The present exercise intervention completely prevented femoral bone loss in premenopausal women while the control patients continued bone loss •No training effect on BMD was observed among postmenopausal patients or at the lumbar spine in neither group •The exercise intervention improved neuromuscular fitness both in pre and postmenopausal women 	
<p>Research Gaps:</p> <ul style="list-style-type: none"> •Endocrine status may modulate bone response to exercise. It is also possible that the chemotherapy-induced amenorrhea may mask the exercise effects on bone. All these issues should be taken in account in planning future exercise intervention studies of breast cancer survivors 	

Uth, J, Hornstrup, T, Christensen, JF, et al. (2016). Efficacy of recreational football on bone health, body composition, and physical functioning in men with prostate cancer undergoing androgen deprivation therapy: 32-week follow-up of the FC prostate randomised controlled trial. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 27: 1507-1518.

Abstract: UNLABELLED: Androgen deprivation therapy (ADT) for prostate cancer (PCa) impairs musculoskeletal health. We evaluated the efficacy of 32-week football training on bone mineral density (BMD) and physical functioning in men undergoing ADT for PCa. Football training improved the femoral shaft and total hip BMD and physical functioning parameters compared to control. **INTRODUCTION:** ADT is a mainstay in PCa management. Side effects include decreased bone and muscle strength and increased fracture rates. The purpose of the present study was to evaluate the effects of 32 weeks of football training on BMD, bone turnover markers (BTMs), body composition, and physical functioning in men with PCa undergoing ADT. **METHODS:** Men receiving ADT >6 months (n = 57) were randomly allocated to a football training group (FTG) (n = 29) practising 2-3 times per week for 45-60 min or to a standard care control group (CON) (n = 28) for 32 weeks. Outcomes were total hip, femoral shaft, femoral neck and lumbar spine (L2-L4) BMD and systemic BTMs (procollagen type 1 amino-terminal propeptide, osteocalcin, C-terminal telopeptide of type 1 collagen). Additionally, physical functioning (postural balance, jump height, repeated chair rise, stair climbing) was evaluated. **RESULTS:** Thirty-two-week follow-up measures were obtained for FTG (n = 21) and for CON (n = 20), respectively. Analysis of mean changes from baseline to 32 weeks showed significant differences between FTG and CON in right (0.015 g/cm²) and left (0.017 g/cm²) total hip and in right (0.018 g/cm²) and left (0.024 g/cm²) femoral shaft BMD, jump height (1.7 cm) and stair climbing (-0.21 s) all in favour of FTG (p < 0.05). No other significant between-group differences were observed. **CONCLUSIONS:** Compared to standard care, 32 weeks of football training improved BMD at clinically important femoral sites and parameters of physical functioning in men undergoing ADT for PCa.

Publication Year: 2016	Addresses Premature Aging Specifically: No
Target Population: 57 men receiving androgen deprivation therapy (ADT) for prostate cancer (PCa)	Type of Intervention: Physical Activity
Description of Intervention: Football training: men were randomly allocated to a football training group (FTG) practicing 2–3 times per week for 45–60 min OR to a standard care control group (CON) for 32 weeks	
Long Term Cancer Effect Addressed: <ul style="list-style-type: none"> •Bone Mineral Density (BMD): total hip, femoral shaft, femoral neck and lumbar spine (L2-L4) •Bone turnover markers (BTMs): procollagen type 1 amino-terminal propeptide, osteocalcin, C-terminal telopeptide of type 1 collagen). •Physical function: postural balance, jump height, repeated chair rise, stair climbing 	
Summary of Main Points: <ul style="list-style-type: none"> •Compared to standard care, 32 weeks of football training improved BMD at clinically important femoral sites (total hip and in right (and left femoral shaft) and parameters of physical functioning (jump height and stair climbing) in men undergoing ADT for PCa •No other significant effects were found 	

Winters-Stone, KM, Dobek, J, Nail, LM, et al. (2013). Impact + resistance training improves bone health and body composition in prematurely menopausal breast cancer survivors: a randomized controlled trial. Osteoporosis international: a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 24: 1637-1646.

Abstract: Our randomized controlled trial in prematurely menopausal breast cancer survivors showed that impact + resistance training prevented increases in percentage of body fat compared with controls and also improved BMD at the hip and prevented BMD loss at the spine among exercise-trained women who were menopausal for >1 year. **INTRODUCTION:** Cancer treatment-related menopause worsens bone health and body composition in breast cancer survivors (BCS). We investigated whether impact + resistance training could improve bone mineral density (BMD), reduce bone turnover, build muscle, and decrease fat mass in BCS with premature menopause. **METHODS:** We conducted a randomized controlled trial in 71 BCS (mean age, 46.5 years) within 5 years of treatment-related menopause. Women were randomly assigned to one of two groups: (1) impact + resistance training (prevent osteoporosis with impact + resistance (POWIR)) or (2) exercise placebo (FLEX) 3x/week for 1 year. Outcomes were hip and spine BMD (in grams per square centimeter) and body composition (percent body fat (%BF) and lean and fat mass (in kilograms)) by DXA and bone turnover markers (serum osteocalcin (in nanograms per milliliter) and urinary deoxypryrodinoline (in nanomoles per milliliter)). **RESULTS:** There were no significant group x time interactions for bone outcomes when using an intent-to-treat approach on the full sample. In analyses restricted to BCS who were menopausal for >=1 year, POWIR increased BMD at the hip and slowed BMD loss at the spine compared with FLEX (femoral neck-POWIR, 0.004 +/- 0.093 g/cm(2) vs. FLEX, -0.010 +/- 0.089 g/cm(2); p < 0.01; spine-POWIR, -0.003 +/- 0.114 g/cm(2) vs. FLEX, -0.020 +/- 0.110 g/cm(2); p = 0.03). POWIR prevented increases in %BF (POWIR, 0.01 % vs. FLEX, 1.3 %; p < 0.04). Women with attendance to POWIR at >=64 % had better improvements in %BF than women attending less often (p < 0.03). **CONCLUSION:** Impact + resistance training may effectively combat bone loss and worsening body composition from premature menopause in BCS.

Publication Year: 2013	Addresses Premature Aging Specifically: Yes
Target Population: 71 breast cancer survivors (BCS) within 5 years of treatment-related menopause	Type of Intervention: Physical Activity
<p>Description of Intervention: Progressive, supervised impact + resistance exercise (prevent osteoporosis with impact + resistance (POWIR)):</p> <ul style="list-style-type: none"> •Supervised classes 2 days a week plus home exercise 1 day a week for 12 months •Trained instructors delivered supervised classes and participants followed a similar training program at home •Resistance and/or impact exercise for moderate to high bone loading forces for 30–60 min/session •Control group (FLEX) performed stretching and relaxation exercises 	
<p>Long Term Cancer Effect Addressed:</p> <ul style="list-style-type: none"> •Bone mineral density (BMD)/bone loss: lumbar spine and femoral neck (DXA) •Bone turnover: serum osteocalcin •Maximal muscle strength of the upper and lower body •Training effects on lymphedema: documented by comparing circumferences between arms measured at the base of the middle finger, wrist, and distal forearm at 0, 3, 6, and 12 months of training 	
<p>Summary of Main Points:</p> <ul style="list-style-type: none"> •Among BCS with recent treatment-related menopause, participation in the exercise program (i.e., POWIR) prevented increases in body fat percentage and was more effective when participation was more frequent •POWIR did not appear to affect either index of bone health; however, the phase of menopause may have masked an underlying benefit of exercise on the skeleton •For women who were a year or more past the onset of menopause, POWIR effectively stopped bone loss at the spine and increased BMD at the hip compared with bone loss at both sites in FLEX participants •An important caveat to the BMD outcomes is that POWIR was only effective in BCS past the acute phase of menopause. The positive influence of exercise on bone mass may be influenced by the estrogen environment 	
<p>Research Gaps:</p> <ul style="list-style-type: none"> •Future studies that include bone as an outcome need to carefully consider time since menopause in the research design and sample determination •The ideal exercise prescription for optimizing body composition in BCS must be determined by appropriately designed trials 	

Zhao, SG, Alexander, NB, Djuric, Z, et al. (2016). Maintaining physical activity during head and neck cancer treatment: results of a pilot controlled trial. Head & neck 38 Suppl 1: E1086-1096.

Abstract: BACKGROUND: Concurrent chemoradiotherapy (concurrent CRT) to treat head and neck cancer is associated with significant reductions of weight, mobility, and quality of life (QOL). An intervention focusing on functional exercise may attenuate these losses. METHODS: We allocated patients to a 14-week functional resistance and walking program designed to maintain physical activity during cancer treatment (MPACT group; n = 11), or to usual care (control group; n = 9). Outcomes were assessed at baseline, and 7 and 14 weeks. RESULTS: Compared to controls, the MPACT participants had attenuated decline or improvement in several strength, mobility, physical activity, diet, and QOL endpoints. These trends were statistically significant (p < .05) in knee strength, mental health, head and neck QOL, and barriers to exercise. CONCLUSION: In this pilot study of patients with head and neck cancer undergoing concurrent CRT, MPACT training was feasible and maintained or improved function and QOL, thereby providing the basis for larger future interventions with longer follow-up. (c) 2015 Wiley Periodicals, Inc. Head Neck 38: E1086-E1096, 2016.

Publication Year: 2016

Addresses Premature Aging Specifically: No

Target Population: Patients 40 years or older with stage II to IV head and neck squamous cell carcinoma who were beginning first-line concurrent chemoradiotherapy (CRT) without surgery

Type of Intervention: Physical Activity

Description of Intervention: •**Functional resistance and walking exercise intervention:** Maintaining physical activity during cancer treatment [MPACT]) intervention: delivered at a clinical research center by a trainer after concurrent CRT initiation up to week 7 (3 sessions per week, lasting up to 1 hour) and then post-concurrent CRT at home, with weekly trainer telephone calls from weeks 8 to 14

•The initial 7-week MPACT program included:

-Functional resistance training: whole body exercises with weights 8 to 12 repetition sets of each functional resistance training exercise by the conclusion of the 7-week training period

-Walking: participants were given a pedometer, and the goal was to maintain step count based on the mean step count of the previous training week. Multiple short duration continuous walking periods were recommended, such as walking for 5 minutes 6 times throughout the day to achieve a total walking time of 30 minutes

•Home program—After the 7-week on-site training, MPACT participants were asked to integrate safe exercise activities into their own lifestyle through home activities. Participants were asked to perform their individualized functional resistance and walking program solely off-site for the last 7 weeks of the study (weeks 8–14)+ weekly trainer telephone call

Long Term Cancer Effect Addressed: •Physical Function: muscle strength (elbow flexion, knee extension, and grip strength; functional mobility (6-minute walk, timed up and go

•Body composition: lean body mass (%) calculated using dual-energy X-ray absorptiometry; BMI

•Concurrent chemoradiotherapy toxicity

Summary of Main Points: •The trial demonstrated the feasibility of a functional resistance and walking exercise intervention (MPACT) provided during 7 weeks of concurrent CRT and during 7 weeks of follow-up

•Compared with controls and in evaluating changes from baseline to 7 and 14 weeks, MPACT participants tended to exhibit less concurrent CRT-induced decline and even some improvement in nearly all measured domains, namely in muscle strength, functional mobility, QOL, sleep disturbance, head and neck-specific QOL, self-reported and objectively assessed physical activity, barriers to exercise, and diet

•Despite the small sample size, statistically significant changes in MPACT versus controls were noted in knee strength, mental health and head and neck QOL, and barriers to exercise

Research Gaps: •Future studies utilizing MPACT will need to explore the importance of cognitive-behavioral support and outcomes

•Exercise programs providing both resistance and walking training might improve muscle strength and functional mobility in patients with head and neck cancer both during and after concurrent CRT, with the suggestion that there is likely to be a degree of training specificity necessary (i.e., walking training to improve walking). Further controlled studies are needed with more prolonged follow-up to evaluate how well these changes are maintained.

Physical Activity Interventions

Reviews

Christensen, JF, Bandak, M, Campbell, A, et al. (2015). Treatment-related cardiovascular late effects and exercise training countermeasures in testicular germ cell cancer survivorship. Acta oncologica (Stockholm, Sweden) 54: 592-599.	
Publication Year: 2015	Type of Review: Narrative Review
<p>Abstract: BACKGROUND: Treatment of testicular germ cell cancer constitutes a major success story in modern oncology. Today, the vast majority of patients are cured by a therapeutic strategy using one or more highly effective components including surgery (orchietomy), radiotherapy and/or chemotherapy. However, the excellent cancer-specific survival comes at considerable costs, as individuals with a history of germ cell cancer experience serious long-term complications, including markedly increased risk of cardiovascular morbidities and premature cardiovascular death. The factors responsible, as well as their mode of action, are not fully understood and there is a lack of knowledge concerning optimal evidence-based long-term follow-up strategies. RESULTS: Here, we present the growing body of evidence suggesting that germ cell cancer patients as a consequence of the different treatment components, are subjected to toxicities, which individually, and synergistically, can cause physiological impairments leading to sub-clinical or clinical cardiovascular disorders (i.e. the 'multiple-hit hypothesis'). Furthermore, we discuss the efficacy and utility of structured exercise training to ameliorate treatment-induced cardiovascular dysfunction to prevent premature onset of clinical cardiovascular disease in germ cell cancer survivors, with a view towards highlighting future directions of exercise-based survivorship research in the germ cell cancer setting. CONCLUSION: As exercise training may have the potential to ameliorate and/or reverse long-term cardiovascular disease sequelae in germ cell cancer survivors, a strong rationale exists for the promotion of exercise oncology research in this setting, in order to provide exercise recommendations for optimal germ cell cancer survivorship.</p>	
Addresses Premature Aging Specifically: No	Target Population: Testicular germ cell cancer patients
Type of Intervention: Physical Activity	
Description of Intervention: Structured exercise training	
Long Term Cancer Effect Addressed: •Treatment-induced cardiovascular dysfunction to prevent premature onset of clinical cardiovascular disease	
<p>Summary of Main Points: •Germ Cell Cancer is highly curable in modern oncology practice, thus the steadily increasing incidence means that an increasing number of individuals will undergo treatment in the future, and in turn be subjected to toxicities leading to increased risk of cardiovascular disease</p> <ul style="list-style-type: none"> •Many of these complications involve negative changes in biological mechanisms, which, under normal circumstances, can be positively moderated by structured exercise •Therefore, a strong rationale exists for the promotion of exercise oncology research in the GCC setting, in order to provide exercise recommendations based on high quality evidence, and ultimately improve GCC survivorship 	
<p>Research Gaps: •Elucidating the long-term implications and underlying mechanisms of tailored exercise training in patients displaying subclinical hypogonadism, and/or undergoing BEP therapy should be prioritized, as these patients present with a significant cardiovascular risk profile</p> <ul style="list-style-type: none"> • Evidence describing which exercise prescriptions (modality, intensity, volume and progression) may be most appropriate after orchietomy, as well as during and after BEP therapy, to reverse acute physiological side effects, is required •In relation to long-term survivorship, there are no studies describing the effect of structured exercise on late occurring disorders, and such interventions will likely need to be of longer duration (6 months) and designed with appropriate progression in the exercise prescription. 	

Daum, CW, Cochrane, SK, Fitzgerald, JD, et al. (2016). exercise interventions for preserving physical function among cancer survivors in middle to late life. The journal of frailty & aging 5: 214-224.	
Publication Year: 2016	Type of Review: Systematic Review
<p>Abstract: The purpose of this review was to evaluate randomized controlled trials aiming to preserve the functional status, i.e. physical capabilities, of middle-aged and older cancer survivors through a structured, physical exercise intervention. The study team performed a thorough search of the literature using six online databases. This literature search limited included studies to randomized controlled trials which implemented a structured physical activity intervention for middle- and older-aged adults diagnosed with cancer. Studies were also required include at least one objective measure of physical function as a dependent outcome. This literature search yielded thirty-eight studies. The majority of the literature reviewed was successful in improving several functional outcomes including time needed to rise from a chair or distance covered during the six-minute walk test. A large number of published trials also suggest that exercise is effective in decreasing fatigue. However, a lack of trials investigating outcomes in older populations (>= 65 years) was noted in this review. The results of this review suggest that a structured exercise program may be physically beneficial for middle-aged to older cancer survivors. Particularly, such interventions could preserve the functional status of cancer patients and, consequently, improve their long-term health outcomes. Future implications include further investigation into strictly older cancer patient populations, as outcomes related to exercise might differ between older and middle-aged adults.</p>	
Addresses Premature Aging Specifically: Yes	Target Population: Middle-aged and older cancer survivors through a structured, physical exercise intervention
Type of Intervention: Physical Activity	
Description of Intervention: Structured exercise interventions to improve physical function	
Long Term Cancer Effect Addressed: •Physical function: different tests (e.g., six-minute walk test, chair rise test)	
Summary of Main Points: •A structured exercise program may be physically beneficial for middle-aged to older cancer survivors. Particularly, such interventions could preserve the functional status of cancer patients and, consequently, improve their long-term health outcomes	
Research Gaps: • A lack of trials investigating outcomes in older populations (≥ 65 years) was noted in this review •Future implications include further investigation into strictly older cancer patient populations, as outcomes related to exercise might differ between older and middle-aged adults	

Focht, BC, Clinton, SK, Devor, ST, et al. (2013). Resistance exercise interventions during and following cancer treatment: a systematic review. The journal of supportive oncology 11: 45-60.	
Publication Year: 2013	Type of Review: Meta-analysis
Abstract: Findings from prior systematic reviews suggest that exercise results in meaningful improvements in many clinically relevant physiologic and quality of life (QOL) outcomes during and following cancer treatment. However, the majority of exercise-cancer studies have focused upon the benefits of aerobic exercise (AE) and knowledge of the efficacy of resistance exercise (RE) alone as a supportive care intervention for cancer patients and survivors remains limited. Consequently, the purpose of this review was to provide the first systematic evaluation of the effects of RE alone upon clinically relevant physiologic and QOL outcomes during and following cancer treatment. Literature searches were conducted to identify studies examining RE interventions in cancer patients and survivors. Data were extracted on physiologic (fitness, physical function, and body composition) and QOL (fatigue, psychological well-being, and cancer-specific and global QOL outcomes). Cohen's d effect sizes were calculated for each outcome. A total of 15 studies (6 in samples undergoing active cancer treatment and 9 in samples having completed cancer treatment) involving 1,077 participants met the inclusion criteria. Findings revealed that, on average, RE resulted in large effect-size improvements in muscular strength (d = 0.86), moderate effect-size improvements in physical function (d = 0.66), and small effect-size improvements in body composition (d = 0.28) and QOL (d = 0.25) outcomes. The effect sizes observed following RE are comparable in magnitude to the effects of exercise interventions reported in prior comprehensive reviews of the exercise-cancer literature which primarily focused upon AE. Additionally, the methodologic quality of the studies was generally strong. Taken collectively, results of this systematic review suggest that RE is a promising supportive care intervention that results in meaningful improvements in clinically relevant physiologic and QOL outcomes during and following cancer treatment.	
Addresses Premature Aging Specifically: No	Target Population: Cancer patients or survivors
Type of Intervention: Physical Activity	
Description of Intervention: Resistance Exercise: regular participation in structured, repetitive strength training program over an extended period of time	
Long Term Cancer Effect Addressed: Physical Function Muscle Strength Body composition Other outcomes: QoL, fatigue	
Summary of Main Points: •Strength training is a safe, feasible intervention that generates significantly large positive effects (clinically meaningful improvements) in muscle strength, moderate effect in physical function and small but significant effects in body composition during and after cancer treatment	
Research Gaps: •Additional randomized control trials are needed to firmly establish the benefits of resistance training for cancer patients and survivors •Future studies should include patients or survivors with different cancer diagnostics, and phases •Future studies should expand the assessment of adherence to resistance training prescription characteristics (sets, reps, load, volume) and the sustained effects of the benefits after the cessation of the intervention	

Fuller, JT, Hartland, MC, Maloney, LT, et al. (2018). Therapeutic effects of aerobic and resistance exercises for cancer survivors: a systematic review of meta-analyses of clinical trials. British journal of sports medicine 52: 1311.	
Publication Year: 2018	Type of Review: Systematic Review
<p>Abstract: OBJECTIVE: To systematically appraise and summaries meta-analyses investigating the effect of exercise compared with a control condition on health outcomes in cancer survivors. DESIGN: Umbrella review of intervention systematic reviews. DATA SOURCES: Web of Science, Scopus, Cochrane Library, CINAHL and MEDLINE databases were searched using a predefined search strategy. ELIGIBILITY CRITERIA: Eligible meta-analyses compared health outcomes between cancer survivors participating in an exercise intervention and a control condition. Health outcomes were cardiovascular fitness, muscle strength, health-related quality of life, cancer-related fatigue and depression. Pooled effect estimates from each meta-analysis were quantified using standardized mean differences and considered trivial (<0.20), small (0.20-0.49), moderate (0.50-0.79) and large (>/=0.80). Findings were summarized using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. RESULTS: There were 65 eligible articles that reported a total of 140 independent meta-analyses. 139/140 meta-analyses suggested a beneficial effect of exercise. The beneficial effect was statistically significant in 104 (75%) meta-analyses. Most effect sizes were moderate for cardiovascular fitness and muscle strength and small for cancer-related fatigue, health-related quality of life and depression. The quality of evidence was variable according to the GRADE scale, with most studies rated low or moderate quality. Median incidence of exercise-related adverse events was 3.5%. CONCLUSION: Exercise likely has an important role in helping to manage physical function, mental health, general well-being and quality of life in people undergoing and recovering from cancer and side effects of treatment. PROSPERO REGISTRATION NUMBER: CRD42015020194.</p>	
Addresses Premature Aging Specifically: No	Target Population: Adults with any cancer diagnosis
Type of Intervention: Physical Activity	
Description of Intervention: Exercise interventions involving aerobic, resistance or combined aerobic and resistance exercises	
<p>Long Term Cancer Effect Addressed: Muscle strength: upper limb, lower limb, and non-specific muscle strength using measurements of peak torque or the maximum mass lifted for a given number of repetitions Depression</p>	
<p>Summary of Main Points: •Strength: Pooled effect estimates from 21 meta-analyses suggested a beneficial effect of exercise on muscle strength in cancer survivors -This beneficial effect was statistically significant in 20/21 (95%) meta-analyses. Most meta-analyses (14/21) reported a moderate or greater effect size and provided moderate (eight meta-analyses) or low (nine meta-analyses) quality of evidence •Pooled effect estimates from 19/20 meta-analyses suggested a beneficial effect of exercise on depression in cancer survivors (i.e., reduced depression; table 5). This beneficial effect was statistically significant in 12/19 (63%) meta-analyses (table 5). Most meta-analyses (12/19) reported a small effect size •Six meta-analyses included only studies investigating resistance exercise and reported a pooled effect estimate that were similar to the remaining meta-analyses, which included a mix of resistance and aerobic exercise studies •Depression: Pooled effect estimates from 19/20 meta-analyses suggested a beneficial effect of exercise on depression in cancer survivors (i.e., reduced depression). This beneficial effect was statistically significant in 12/19 (63%) meta-analyses. Most meta-analyses (12/19) reported a small effect size</p>	
<p>Research Gaps: •This umbrella review were based entirely or mostly on studies undertaken in breast cancer survivors. Therefore, future research investigating exercise in cancer survivors should seek to include survivors of other types of cancer. •There needs to be increased emphasis on primary research studies investigating exercise in cancer survivors rather than additional meta-analyses. Our umbrella review identified over 90 meta-analyses across over 40 systematic reviews published in the last 5 years. It is questionable how much new knowledge can be generated from further meta-analyses on this topic until more primary studies have been completed</p>	

Swartz, MC, Lewis, ZH, Lyons, EJ, et al. (2017). Effect of home- and community-based physical activity interventions on physical function among cancer survivors: a systematic review and meta-analysis. Archives of physical medicine and rehabilitation 98: 1652-1665.	
Publication Year: 2017	Type of Review: Meta-analysis
Abstract: OBJECTIVE: To examine the effect of home- and community-based physical activity interventions on physical functioning among cancer survivors based on the most prevalent physical function measures, randomized trials were reviewed. DATA SOURCES: Five electronic databases-Medline Ovid, PubMed, CINAHL, Web of Science, and PsycINFO-were searched from inception to March 2016 for relevant articles. STUDY SELECTION: Search terms included community-based interventions, physical functioning, and cancer survivors. A reference librarian trained in systematic reviews conducted the final search. DATA EXTRACTION: Four reviewers evaluated eligibility and 2 reviewers evaluated methodological quality. Data were abstracted from studies that used the most prevalent physical function measurement tools-Medical Outcomes Study 36-Item Short-Form Health Survey, Late-Life Function and Disability Instrument, European Organisation for the Research and Treatment of Cancer Quality-of-Life Questionnaire, and 6-minute walk test. Random- or fixed-effects models were conducted to obtain overall effect size per physical function measure. DATA SYNTHESIS: Fourteen studies met inclusion criteria and were used to compute standardized mean differences using the inverse variance statistical method. The median sample size was 83 participants. Most of the studies (n=7) were conducted among breast cancer survivors. The interventions produced short-term positive effects on physical functioning, with overall effect sizes ranging from small (.17; 95% confidence interval [CI], .07-.27) to medium (.45; 95% CI, .23-.67). Community-based interventions that met in groups and used behavioral change strategies produced the largest effect sizes. CONCLUSIONS: Home and community-based physical activity interventions may be a potential tool to combat functional deterioration among aging cancer survivors. More studies are needed among other cancer types using clinically relevant objective functional measures (eg, gait speed) to accelerate translation into the community and clinical practice.	
Addresses Premature Aging Specifically: Yes	Target Population: Adult cancer survivors
Type of Intervention: Physical Activity	
Description of Intervention: 3 main types of physical activity interventions <ul style="list-style-type: none"> •Behavioral change exercise interventions: based on the Transtheoretical model, Social Cognitive Theory, Motivational Readiness, and a combination of stages of readiness with motivational interviewing principles -in-person counseling or group-based sessions •Home-based exercise interventions: Strength and/or aerobic exercise •Supervised exercise interventions: individual or in group in a community facility -Supervision was either in conjunction with home-based exercise or preceded the home-based exercise maintenance portion of the intervention -All the studies in this section prescribed supervised exercise twice a week 	
Long Term Cancer Effect Addressed: •Physical function: different tests including the SF-36) physical-function subscale, Late Life Function and Disability Instrument (LLFDI), European Organization for the Research and Treatment of Cancer Quality-of-Life questionnaire—Core 30 (EORTC QLQ-C30)	
Summary of Main Points: •Home and community-based physical activity interventions had a positive effect on four out of the five mobility and performance capacity measures in cancer survivors, despite the variability among individual studies. <ul style="list-style-type: none"> •The interventions produced a small to moderate positive effect on physical functioning in cancer survivors •Interventions differed widely in regards to type of exercise intervention (aerobic, resistance, or weight training), duration (12 to 52 weeks), number of sessions (3 to 104 session), and settings (home, group, or combinations) •Community-based interventions that met in groups and used cognitive behavioral therapy may be the most effective physical activity intervention format for improving physical functioning among cancer survivors 	
Research Gaps: •Studies will need to include objective mobility, performance capacity, and physical activity measures more consistently in order to strengthen the evidence supporting the use of home and community-based physical activity interventions by clinicians as an additional method to help improve physical functioning in cancer survivors	

Toohy, K, Pampa, K, McKune, A, et al. (2018). High-intensity exercise interventions in cancer survivors: a systematic review exploring the impact on health outcomes. Journal of cancer research and clinical oncology 144: 1-12.	
Publication Year: 2018	Type of Review: Systematic Review
<p>Abstract: PURPOSE: There is an increasing body of evidence underpinning high-intensity exercise as an effective and time-efficient intervention for improving health in cancer survivors. The aim of this study was to, (1) evaluate the efficacy and (2) the safety of high-intensity exercise interventions in improving selected health outcomes in cancer survivors. METHODS: Design Systematic review. Data sources Google Scholar and EBSCO, CINAHL Plus, Computers and Applied Sciences Complete, Health Source-Consumer Edition, Health Source: Nursing/Academic Edition, MEDLINE, Web of Science and SPORTDiscuss from inception up until August 2017. Eligibility criteria Randomized controlled trials of high-intensity exercise interventions in cancer survivors (all cancer types) with health-related outcome measures. The guidelines adopted for this review were the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). RESULTS: The search returned 447 articles, of which nine articles (n = 531 participants mean, age 58 +/- 9.5 years) met the eligibility criteria. Exercise interventions of between 4 and 18 weeks consisting of high-intensity interval bouts of up to 4-min were compared with a continuous moderate intensity (CMIT) intervention or a control group. High-intensity exercise interventions elicited significant improvements in VO2 max, strength, body mass, body fat and hip and waist circumference compared with CMIT and/or control groups. The studies reviewed showed low risk in participating in supervised high-intensity exercise interventions. Mixed mode high-intensity interventions which included both aerobic and resistance exercises were most effective improving the aerobic fitness levels of cancer survivors by 12.45-21.35%, from baseline to post-intervention. CONCLUSION: High-intensity exercise interventions improved physical and physiological health-related outcome measures such as cardiovascular fitness and strength in cancer survivors. Given that high-intensity exercise sessions require a shorter time commitment, it may be a useful modality to improve health outcomes in those who are time poor. The risk of adverse events associated with high-intensity exercise was low.</p>	
Addresses Premature Aging Specifically: No	Target Population: Cancer survivors
Type of Intervention: Physical Activity	
Description of Intervention: High-intensity exercise interventions: included studies compared high-intensity interval bouts of up to 4-min (followed by active recovery bouts) with a continuous moderate intensity (CMIT) intervention or a control group	
Long Term Cancer Effect Addressed: <ul style="list-style-type: none"> •Body composition: body mass, body fat and hip and waist circumference •Fitness: VO2 max, strength 	
<p>Summary of Main Points:</p> <ul style="list-style-type: none"> •High-intensity exercise interventions improved physical and physiological health-related outcome measures such as cardiovascular fitness and strength in cancer survivors •Given that high-intensity exercise sessions require a shorter time commitment, it may be a useful modality to improve health outcomes in those who are time poor •The risk of adverse events associated with high-intensity exercise was low •Mixed mode high-intensity interventions which included both aerobic and resistance exercises were most effective improving the aerobic fitness levels of cancer survivors 	

Nutrition Interventions

Original Research

<p>Paur, I, Lilleby, W, Bohn, SK, et al. (2017). Tomato-based randomized controlled trial in prostate cancer patients: effect on PSA. Clinical nutrition (Edinburgh, Scotland) 36: 672-679.</p>	
<p>Abstract: BACKGROUND & AIMS: The effect of lycopene-containing foods in prostate cancer development remains undetermined. We tested whether a lycopene-rich tomato intervention could reduce the levels of prostate specific antigen (PSA) in prostate cancer patients. METHODS: Prior to their curative treatment, 79 patients with prostate cancer were randomized to a nutritional intervention with either 1) tomato products containing 30 mg lycopene per day; 2) tomato products plus selenium, omega-3 fatty acids, soy isoflavones, grape/pomegranate juice, and green/black tea (tomato-plus); or 3) control diet for 3 weeks. RESULTS: The main analysis, which included patients in all risk categories, did not reveal differences in changes of PSA-values between the intervention and control groups. Post-hoc, exploratory analyses within intermediate risk (n = 41) patients based on tumor classification and Gleason score post-surgery, revealed that median PSA decreased significantly in the tomato group as compared to controls (-2.9% and +6.5% respectively, p = 0.016). In separate post-hoc analyses, we observed that median PSA-values decreased by 1% in patients with the highest increases in plasma lycopene, selenium and C20:5 n-3 fatty acid, compared to an 8.5% increase in the patients with the lowest increase in lycopene, selenium and C20:5 n-3 fatty acid (p = 0.003). Also, PSA decreased in patients with the highest increase in lycopene alone (p = 0.009). CONCLUSIONS: Three week nutritional interventions with tomato-products alone or in combination with selenium and n-3 fatty acids lower PSA in patients with non-metastatic prostate cancer. Our observation suggests that the effect may depend on both aggressiveness of the disease and the blood levels of lycopene, selenium and omega-3 fatty acids.</p>	
<p>Publication Year: 2017</p>	<p>Addresses Premature Aging Specifically: No</p>
<p>Target Population: 79 Patients with localized prostate cancers</p>	<p>Type of Intervention: Nutrition</p>
<p>Description of Intervention: Tomato based lycopene-rich diet: patients were randomized to: a tomato group, and a tomato-plus group or control</p> <ul style="list-style-type: none"> •Tomato group: included tomato products with a content of 30 mg lycopene per day (e.g., Pasta sauce, tomato juice, crushed tomatoes) •Tomato-plus: included tomato products PLUS green tea (a cup) and black tea (a cup), pomegranate and grape juice (330 mL of each), 200mg soy isoflavones, 200 mg 1-selenomethionin and 3.13 g n-3 fatty acids per day •Control group: encouraged to continue their habitual diet 	
<p>Long Term Cancer Effect Addressed: •Levels of prostate specific antigen (PSA) (biomarker associated with cancer progression)</p>	
<p>Summary of Main Points: •Daily consumption of tomato products containing 30 mg lycopene for 3 weeks may reduce PSA values in intermediate risk prostate cancer patients. The indication of reduced PSA increase in intermediate risk prostate cancer patients by tomato products warrants further investigation</p> <ul style="list-style-type: none"> •The main analysis, which includes all patients, revealed no differences in PSA changes in intervention groups compared to the control group. However, it is possible that the study ended up underpowered for this primary analysis due to a lower than expected initial consent rate •In a separate post-hoc analysis, subjects with intermediate risk prostate cancers in the post-surgery risk reclassification had significant reduction in PSA in the tomato group as compared to the control group 	
<p>Research Gaps: •Daily consumption of lycopene-rich tomato products may affect PSA values in prostate cancer patients with intermediate risk profiles however this finding needs to be confirmed in RCTs</p>	

Nutrition Interventions

Reviews

Harvie, MN, Howell, T. (2016). Could intermittent energy restriction and intermittent fasting reduce rates of cancer in obese, overweight, and normal-weight subjects? A summary of evidence. Advances in nutrition (Bethesda, Md) 7: 690-705.	
Publication Year: 2016	Type of Review: Narrative Review
<p>Abstract: Animal studies and human observational data link energy restriction (ER) to reduced rates of carcinogenesis. Most of these studies have involved continuous energy restriction (CER), but there is increasing public and scientific interest in the potential health and anticancer effects of intermittent energy restriction (IER) or intermittent fasting (IF), which comprise periods of marked ER or total fasting interspersed with periods of normal eating. This review summarizes animal studies that assessed tumor rates with IER and IF compared with CER or ad libitum feed consumption. The relevance of these animal data to human cancer is also considered by summarizing available human studies of the effects of IER or IF compared with CER on cancer biomarkers in obese, overweight, and normal-weight subjects. IER regimens that include periods of ER alternating with ad libitum feed consumption for 1, 2, or 3 wk have been reported to be superior to CER in reducing tumor rates in most spontaneous mice tumor models. Limited human data from short-term studies (</=6 mo) in overweight and obese subjects have shown that IER can lead to greater improvements in insulin sensitivity (homeostasis model assessment) than can CER, with comparable reductions in adipokines and inflammatory markers and minor changes in the insulin-like growth factor axis. There are currently no data comparing IER or IF with CER in normal-weight subjects. The benefits of IER in these short-term trials are of interest, but not sufficient evidence to recommend the use of IER above CER. Longer-term human studies of adherence to and efficacy and safety of IER are required in obese and overweight subjects, as well as normal-weight subjects.</p>	
Addresses Premature Aging Specifically: No	Target Population: Obese, overweight, and normal weight subjects
Type of Intervention: Nutrition	
Description of Intervention: Intermittent energy restriction (IER) or intermittent fasting (IF): comprise periods of marked ER or total fasting interspersed with periods of normal eating	
Long Term Cancer Effect Addressed: Cancer Risk/ tumor development	
<p>Summary of Main Points:</p> <ul style="list-style-type: none"> •Preliminary data has showed potential benefits on cancer risk biomarkers that are thought to mediate the links between adiposity and energy intake and the development and growth of cancers, including insulin, IGF-I, leptin, adiponectin, cytokines, and inflammation-related molecules •The limited data on IER and IF show some, but by no means consistent, beneficial effects, and are currently insufficient to support claims about the anticancer effects of IER and IF. However, the popularity of intermittent dieting and some positive findings with IER compared with continuous energy restriction mean IER deserves further study 	
<p>Research Gaps:</p> <ul style="list-style-type: none"> •There are no data, to our knowledge, on the effects of IER and IF on cancer rates in humans •Human studies of IER and IF mainly have been short-term, and involved small groups of selected subjects. These studies do not inform about any potential longer-term adaptations and effects on disease risk with longer-term IER or IF that may occur. Longer-term studies (>6 mo) of adherence to and efficacy and safety of IER and IF are required in obese, overweight, and normal-weight subjects •High-quality research comparing IER and IF with continuous energy restriction are required to ascertain any true health benefits and anticancer effects 	

O'Flanagan, CH, Smith, LA, McDonell, SB, et al. (2017). When less may be more: calorie restriction and response to cancer therapy. BMC medicine 15: 106.

Publication Year: 2017

Type of Review: Narrative Review

Abstract: Calorie restriction (CR) extends lifespan and has been shown to reduce age-related diseases including cancer, diabetes, and cardiovascular and neurodegenerative diseases in experimental models. Recent translational studies have tested the potential of CR or CR mimetics as adjuvant therapies to enhance the efficacy of chemotherapy, radiation therapy, and novel immunotherapies. Chronic CR is challenging to employ in cancer patients, and therefore intermittent fasting, CR mimetic drugs, or alternative diets (such as a ketogenic diet), may be more suitable. Intermittent fasting has been shown to enhance treatment with both chemotherapy and radiation therapy. CR and fasting elicit different responses in normal and cancer cells, and reduce certain side effects of cytotoxic therapy. Findings from preclinical studies of CR mimetic drugs and other dietary interventions, such as the ketogenic diet, are promising for improving the efficacy of anticancer therapies and reducing the side effects of cytotoxic treatments. Current and future clinical studies will inform on which cancers, and at which stage of the cancer process, CR, fasting, or CR mimetic regimens will prove most effective.

Addresses Premature Aging Specifically: Yes

Target Population: Cancer patients

Type of Intervention: Nutrition

Description of Intervention: Calorie restriction (CR): a chronic reduction of dietary energy intake by approximately 30% without incurrance of malnutrition

Long Term Cancer Effect Addressed: Cancer prevention

Summary of Main Points:

- Caloric Restriction (CR) is an established tumor preventative regimen, reducing systemic inflammation and growth factor signaling, as well as improving metabolic markers
- Improved metabolism and inflammation are also likely mechanisms through which CR may reduce tumor growth and enhance therapeutic response
- As chronic CR is contraindicated for many cancer patients at risk for weight loss, cachexia, and immunosuppression, intermittent CR, fasting-mimicking diets, low carbohydrate/ketogenic diets, or CR mimetic drugs may be more suitable
- Fasting and low carbohydrate diets have been shown to reduce side effects and to improve chemotherapy and radiation therapy in animal models, and there is great promise for these interventions in the clinic

Research Gaps:

- Preclinical studies are mounting on the effects of intermittent CR in combination with chemotherapy and radiation therapy, clinical studies are slow to follow, likely due to concerns such as potential interference of CR on delivery of therapeutic drugs to the tumor cells
- More preclinical studies are required to determine in which cancers, at which stage, and in what combinations CR mimetic drugs may prove most effective
- Future studies should take into consideration (1) the risk of cachexia in a patient population, whereby those at high risk may benefit from a ketogenic diet or short-term fasting; (2) the immunologic state of the enrolled patients, when CR or rapamycin treatment may be detrimental to wound healing or inflammatory responses; and (3) the metabolic state of patients, with diabetic patients in particular being at risk of adverse effects during chronic CR or fasting regimens, whereby treatment with metformin or a ketogenic diet may be of benefit
- While in the short-term studies will need to focus on the safety and added benefit to current therapies, future studies may also focus on the potential of CR in enhancing the response to lower doses of chemotherapy and radiation therapy

Multicomponent Interventions

Original Research

Arikawa, AY, Kaufman, BC, Raatz, SK, et al. (2018). Effects of a parallel-arm randomized controlled weight loss pilot study on biological and psychosocial parameters of overweight and obese breast cancer survivors. Pilot and feasibility studies 4: 17.

Abstract: BACKGROUND: Weight gain often occurs after breast cancer (BC) diagnosis and obesity along with sedentary behavior are associated with increased risk of BC recurrence and mortality. The primary objective of this study was to determine whether a significant weight loss, of approximately 10%, would lead to beneficial changes in biomarkers associated with cancer and/or cancer recurrence, and quality of life (QOL) in overweight and obese BC survivors. METHODS: This parallel-arm study took place in Minneapolis, Minnesota, from January 2009 until March 2010. Participants were overweight and obese postmenopausal BC survivors who had completed treatment at least 3 months prior to enrollment and who did not smoke. Twenty-one BC survivors were randomized, via a random number generator computer software, to a 1000-calorie deficit feeding and exercise intervention (CR) or a weight management counseling intervention (WM) for 12 weeks followed by a 6-week follow-up. Body weight, biomarkers, and QOL were measured at baseline, weeks 6, 12, and 18. Body composition and fitness level were measured at only two time points. RESULTS: Twenty-one women were enrolled into the study and 20 completed all time points. Weight loss occurred with both interventions. Body weight in CR changed from 85.5 (95% confidence interval (CI) 77, 94) kg to 76.7 (95% CI 68.1, 85.2) kg, whereas in WM it changed from 98.3 (95% CI 89.8, 106.8) kg to 93.2 (95% CI 84.6, 101.7) kg. Fitness in CR changed from 4.9 (95% CI 4, 5.8) to 6.3 (95% CI 5.4, 7.2). CR led to lower plasma levels of leptin, F2-isoprostanes, and CRP. Quality of life seemed to improve with both interventions, while sleep quality decreased only in CR. CONCLUSIONS: Overweight and obese BC survivors were able to adhere to a strict diet and exercise program, which significantly decreased body weight, increased fitness level, and improved biomarkers and QOL. However, the strict dietary intervention in CR seemed to decrease participants' sleep quality and social relationships. Future larger randomized controlled trials should focus on behavioral modification and personalized nutrition counseling to help breast cancer survivors achieve a sustainable weight loss and fitness level.

Publication Year: 2018	Addresses Premature Aging Specifically: No
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Target Population: Overweight and obese women who were breast cancer survivors	Type of Intervention: Multicomponent
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Description of Intervention: Weight loss interventions (Diet and Physical Activity):

- Diet plus exercise based weight loss intervention (CR): Women were provided freshly prepared meals for 12 weeks (breakfast, lunch, dinner, and a snack reflecting a deficit of 600–900 kcal per day)
- Women had a progressive exercise intervention: aerobic and strength training, and a membership to a fitness center
- Exercise was supervised by a certified trainer, who met with each participant 2x week for the first 4 weeks, and once per week thereafter
- A weight management counseling intervention (WM): weekly 1-h weight management classes supervised by a registered dietitian for 12 weeks
- Individualized guidelines for the energy-restricted diet, menu plans, and topics related to short-term and long-term weight loss, including exercise and behavior modification

Long Term Cancer Effect Addressed:

- Body composition (DXA)
- Fitness
- Cancer-related biomarkers
- HRQoL

Summary of Main Points:

- Women in both groups successfully lost weight and percent body fat during the trial. However, women in CR lost more weight and %BF compared to WM at weeks 6, 12, and 18
- CR also had a significantly greater increase in fitness compared to baseline and also compared to WM
- Both groups were able to maintain or continue to reduce body weight during the limited contact follow-up (weeks 12–18), although the CR participants showed greater weight loss and greater improvements in fitness level at week 18

- A 10% decrease in body weight and a 16% decrease in fat mass were accompanied by improvements in several biomarkers that may translate into lower recurrence, morbidity, and mortality risks
- Overweight and obese BC survivors were able to adhere to a strict diet and exercise program, which significantly decreased body weight, increased fitness level, and improved biomarkers and QOL. However, the strict dietary intervention in CR seemed to decrease participants' sleep quality and social relationships

Research Gaps: •Future larger randomized controlled trials are needed to determine how to sustain long-term weight loss and fitness and how these can significantly affect prognosis of breast cancer and mortality from a psychosocial perspective as well as a biological perspective, particularly considering systemic biomarkers such as plasma F2-isoprostanes, C-reactive protein, insulin, IGF-1, IGFBP-3, and 25(OH)-vitamin D

- It is also important to determine whether there is an optimal level of weight loss and exercise level that should be sustained over time to reduce recurrence and improve prognosis in breast cancer survivors

Blair, CK, Morey, MC, Desmond, RA, et al. (2014). Light-intensity activity attenuates functional decline in older cancer survivors. *Medicine and science in sports and exercise* 46: 1375-1383.

Abstract: UNLABELLED: While moderate- to vigorous-intensity physical activities (MVPA) confer the greatest health benefits, evidence suggests that light-intensity activities are also beneficial, particularly for older adults and individuals with moderate to severe comorbidities. **PURPOSE:** To examine cross-sectional and longitudinal associations between light-intensity activity and physical function in older cancer survivors at increased risk for age- and treatment-related comorbidities, including accelerated functional decline. **METHODS:** The analysis included data from 641 breast, prostate, and colorectal cancer survivors (54% female) age 65 yr and older who participated in a 1-yr home-based diet and exercise intervention designed to reduce the rate of physical function decline. ANCOVA was used to compare means of physical function across levels of PA intensity (low-light [LLPA]: 1.5-2.0 METs; high-light [HLLPA]: 2.1-2.9 METs; MVPA: \geq 3.0 METs). **RESULTS:** In cross-sectional analyses, increasing tertiles of light-intensity activity were associated with higher scores for all three measures of physical function (all P values <0.005), after adjusting for age, sex, body mass index, comorbidity, symptoms, and MVPA. Associations were stronger for HLLPA than for LLPA. Compared with survivors who had decreased MVPA or maintained stable MVPA and HLLPA at the postintervention follow-up, those who had increased HLLPA, but had decreased MVPA or maintained stable MVPA, reported higher physical function scores (LS means [95% confidence interval]: SF-36 Physical Function Subscale: -5.58 [-7.96 to -3.20] vs -2.54 [-5.83 to 0.75], P = 0.14; Basic Lower Extremity Function: -2.00 [-3.45 to -0.55] vs 0.28 [-1.72 to 2.28], P = 0.07; Advanced Lower Extremity Function: -2.58 [-4.00 to -1.15] vs 0.44 [-1.52 to 2.40], P = 0.01). **CONCLUSIONS:** Our findings suggest that increasing light-intensity activities, especially HLLPA, may be a viable approach to reducing the rate of physical function decline in individuals who are unable or reluctant to initiate or maintain adequate levels of moderate-intensity activities.

Publication Year: 2014

Addresses Premature Aging Specifically: Yes

Target Population: 641 overweight or obese breast, prostate, and colorectal cancer survivors aged 65 and older who participated in a 1-year intervention

Type of Intervention: Multicomponent

Description of Intervention: Diet and exercise intervention: Analysis using data from the RENEW trial, a randomized controlled trial designed to evaluate whether a year-long, diet and exercise intervention:

- Personalized workbook with recommendations for a healthy, calorie-restricted diet and exercise
- Telephone counseling (15 sessions), automated prompts (N=8), and quarterly progress reports
- Participants received a pedometer, resistance exercise bands, a poster with lower-extremity strength training exercises, the Portion Doctor® table guide to food portioning, the T-Factor 2000© fat gram book, and food and activity record logs

Long Term Cancer Effect Addressed: • Physical function: Self-reported using the Physical Function subscale (10 items) of the Short-Form 36 Health Status Survey (SF-36), the Basic and Advanced Lower Extremity Function subscales of the Late Life Function and Disability Index, and the Basic and self-reported level of difficulty in performing basic (e.g., washing dishes while standing, getting into and out of a car) and advanced functional activities

Summary of Main Points: • Light physical activity (LPA) including low-light activities (LLPA); e.g., playing board games, arts and crafts) and high-light activities (HLLPA) involving a combination of standing, ambulatory movement, and upper body movement watering plants) were associated (specially HLLPA) with higher scores for all three measures of physical function

Research Gaps: • More research, particularly interventions and observational studies with longitudinal data, is needed to evaluate the effects of LPA, and especially HLLPA, on physical function.

- Future research involving PA should include the assessment of both exercise and nonexercise PA across the intensity continuum, including both objective and subjective measures.
- Activity monitors with both accelerometer and inclinometer (detects change in posture) functionality, such as the ActivPal3 (PAL Technologies LTD, Glasgow, UK), would enable accurate measurement of sedentary behavior, LPA, and MVPA
- Research is needed to determine the effectiveness of exercise prescriptions to increase HLLPA in terms of initiation, sustainability, as well as short- and long-term effects on physical functioning and other health outcomes

Campbell, KL, Van Patten, CL, Neil, SE, et al. (2012). Feasibility of a lifestyle intervention on body weight and serum biomarkers in breast cancer survivors with overweight and obesity. Journal of the academy of nutrition and dietetics 112: 559-567.

Abstract: Physical inactivity and being overweight or obese are lifestyle factors that put breast cancer survivors at a higher risk for a cancer recurrence and/or development of other chronic diseases. Despite this, there is limited research that has identified effective lifestyle interventions aimed specifically at weight loss in breast cancer survivors. This pilot study is a single-arm experimental pre-post test design, conducted from November 2009 to July 2010, that tested the efficacy of a 24-week group-based lifestyle intervention modeled on the Diabetes Prevention Program in early stage breast cancer survivors (N=14). The intervention included 16 diet sessions led by a registered dietitian and 150 min/wk of moderate-to-vigorous exercise. Study outcome measures were completed at baseline, 24, and 36 weeks (nonintervention follow-up). The primary outcome was change in body weight, and secondary outcomes were change in body composition, aerobic fitness, dietary intake, and blood biomarkers. Overall, participants were postmenopausal women aged 54.6+/-8.3 years with obesity (body mass index 30.1+/-3.6), and had completed adjuvant cancer treatment 2 years prior. Results showed an average weight loss of 3.8+/-5.0 kg and a decrease in body mass index, percent body fat, and waist and hip circumferences at 24 weeks and an additional mean weight loss of 0.8+/-1.2 kg at 36 weeks. In exploratory analysis, participants who lost >7% body weight were older and attended a greater percentage of diet and supervised exercise sessions. There were no significant changes in any of the blood biomarkers at 24 and 36 weeks; however, the results provide a measure of expected effect size for future research studies. This pilot study demonstrated the efficacy of a lifestyle intervention based on the Diabetes Prevention Program in early stage breast cancer survivors and represents an innovative clinical intervention for dietetics practitioners to address the unmet need for programs.

Publication Year: 2012	Addresses Premature Aging Specifically: No
Target Population: Women, older than age 18 years, BMI 25 to 35, diagnosed with Stage I to IIIa breast cancer within the past 5 years, completed adjuvant treatment (chemotherapy and/or radiation therapy) for at least 3 months	Type of Intervention: Multicomponent

Description of Intervention: Weight loss diet and exercise intervention: 24-week group-based intervention on diet and exercise

- Diet: 16 group-based sessions following the Diabetes Prevention Program (DPP) curriculum
- Exercise: telephone-based counseling to promote a homebased program of 150 minutes/week of moderate-intensity physical activity, such as brisk walking

-Participants completed two supervised 45-minute exercise sessions per week for 24 weeks at a dedicated research fitness facility, and were asked to complete additional home-based exercise to achieve a total of 150 minutes per week of moderate to vigorous aerobic exercise

Long Term Cancer Effect Addressed: •Body composition: Total fat mass (kg), Lean body mass (kg)
 •Other outcomes: weight loss, dietary intake, VO2 max, HRQoL, blood markers

Summary of Main Points: •At 24-weeks there was a decrease in total fat mass (-3 3.7 kg; P 0.01), percent body fat (-2.4 2.7%; P 0.01), and lean body mass (-0.6 1.9 kg; P 0.001)

- This pilot study demonstrated the feasibility and preliminary efficacy of a lifestyle intervention program in breast cancer survivors with overweight and obesity delivered in a similar setting to an outpatient cancer center
- Using a modified-DPP weight loss intervention, clinically significant improvements were demonstrated for body weight and aerobic fitness, with modest improvements in body composition

Research Gaps: None reported by authors

Demark-Wahnefried, W, Colditz, GA, Rock, CL, et al. (2015). Quality of life outcomes from the Exercise and Nutrition Enhance Recovery and Good Health for You (ENERGY)-randomized weight loss trial among breast cancer survivors. Breast cancer research and treatment 154: 329-337.

Abstract: Obesity is a poor prognostic factor and is negatively related to quality of life (QOL) in breast cancer survivors. Exercise and Nutrition to Enhance Recovery and Good Health for You is the largest weight loss trial completed among cancer survivors. Percent losses in body weight with an intensive group-based intervention versus an attention control were 6.0 versus 1.5 % ($p < 0.0001$) and 3.7 versus 1.3 % ($p < 0.0001$) at 12 and 24 months, respectively. ENERGY also was designed to answer the research question: Does weight loss significantly improve vitality and physical function (key components of QOL)? 692 breast cancer survivors (BMI: 25-45 kg/m²) at 4 US sites were randomized to a year-long intensive intervention of 52 group sessions and telephone counseling contacts versus a non-intensive (control) of two in-person counseling sessions. Weight, self-reported QOL, and symptoms were measured semi-annually for two years. Significant decreases in physical function and increases in symptoms were observed among controls from baseline to 6 months, but not in the intervention arm, -3.45 (95 % Confidence Interval [CI] -6.10, -0.79, $p = 0.0109$) and 0.10 (95 %CI 0.04, 0.16, $p = 0.0021$), respectively. Improvements in vitality were seen in both arms but trended toward greater improvement in the intervention arm -2.72 (95 % CI -5.45, 0.01, $p = 0.0508$). These differences diminished over time; however, depressive symptoms increased in the intervention versus control arms and became significant at 24 months, -1.64 (95 % CI -3.13, -0.15, $p = 0.0308$). Increased QOL has been reported in shorter term diet and exercise trials among cancer survivors. These longer term data suggest that diet and exercise interventions improve some aspects of QOL, but these benefits may diminish over time.

Publication Year: 2015	Addresses Premature Aging Specifically: No
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Target Population: Women (age 21 years) with a history of stage I, II, or III breast cancer diagnosed within the previous 5 years; enrollees must have completed treatment (exception: endocrine therapy), be overweight or obese (BMI 25-45 kg/m)	Type of Intervention: Multicomponent
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Description of Intervention: Weight loss diet and exercise intervention: The Exercise and Nutrition to Enhance Recovery and Good health for You (ENERGY) trial:

- All women received written materials and were counseled to reduce their weight and adhere to dietary and physical activity guidelines of the American Cancer Society
- Intensive program: four months of weekly one-hour group sessions tapering to fortnightly for 2 months and then monthly from 6 months to 1 year; personalized guidance delivered via telephone and/or email in between each of these group sessions; mailed newsletters on a quarterly basis from 6 to 24 months (individually tailored based on current information about physical activity, dietary intake, weight, and overcoming barriers to regulating energy balance)

Long Term Cancer Effect Addressed:

- Physical Function: SF36 subscale
- Other outcomes: vitality, weight loss, depression

Summary of Main Points:

- While the intensive, group based intervention was effective in promoting weight loss, only transitory improvements in physical functioning and symptoms resulted: between-arm differences diminished more rapidly over time, rather than being largely sustained over the two-year study period
- Changes in body weight were directly associated with changes in physical function
- The intensive intervention also was associated with increasing depressive symptomatology
- Data from the ENERGY trial corroborate the variable impact that weight loss interventions have on QOL and psychosocial endpoints

Research Gaps:

- Future research should effectively triage patients to programs that address their particular needs, given the effects of recidivism that often occurs on these interventions
- More research is needed to develop programs that effectively promote weight loss and maintenance in substantial sub-populations of survivors who may need additional support or other interventions
- More lifestyle intervention trials should address long-term changes in behavior and outcomes as ENERGY

Kenzik, KM, Morey, MC, Cohen, HJ, et al. (2015). Symptoms, weight loss, and physical function in a lifestyle intervention study of older cancer survivors. Journal of geriatric oncology 6: 424-432.	
Abstract: OBJECTIVES: Many older cancer survivors are overweight or obese, with additional illness burden increasing functional decline, which may affect their ability to engage in lifestyle interventions. This study examined how overweight long-term survivors' symptom severity associated with comorbidity prior to a diet and exercise intervention was associated with post-intervention function and examined symptoms' effects on function through change in physical activity, diet quality, and weight status. MATERIALS AND METHODS: This is a secondary data analysis of 514 breast, prostate, and colorectal cancer survivors who participated in the one-year home-based diet and exercise intervention Reach-Out to Enhance Wellness trial. Measures included symptoms, weight, physical activity, diet quality, overall physical function (PF), and basic and advanced lower extremity function (BLEF and ALEF). Simple and serial mediation analyses were conducted to examine direct effects of symptom severity on PF, BLEF, and ALEF and indirect effects of symptom severity through changes in diet quality, physical activity, and weight. RESULTS: Symptom severity was directly associated with lower functioning scores for PF (b=-0.63 p<0.001), BLEF (b=-0.33, p<0.001), and ALEF (b=-0.22, p<0.001). Indirect effects of symptom severity through weight loss, physical activity, and diet were not significant. Weight loss and physical activity were associated with higher PF and ALEF and diet quality was associated with higher BLEF. CONCLUSION: Symptom severity of older, overweight cancer survivors negatively affects physical function. However, greater weight loss and more physical activity were associated with higher functioning scores, regardless of symptom severity.	
Publication Year: 2015	Addresses Premature Aging Specifically: Yes
Target Population: Older (≥ 65) obese and overweight breast, prostate, and colorectal cancer survivors	Type of Intervention: Multicomponent
Description of Intervention: Diet and exercise intervention: The Reach-Out to Enhance Wellness (RENEW) trial, 12-month home-based diet-exercise intervention - Tailored mailed-print materials (personalized workbooks as well as exercise and diet “tools” (i.e., resistance bands, tableware to enhance portion control) designed to assist survivors in meeting national guidelines - Telephone counseling: Provided to help survivors overcome barriers to change and monitor change	
Long Term Cancer Effect Addressed: Physical Function: SF-36 (overall function), basic lower extremity function (BLEF) and advanced lower extremity function	
Summary of Main Points: <ul style="list-style-type: none"> • Symptom severity among older, overweight cancer survivors negatively affected all aspects of physical functioning • Despite the symptom burden experienced by older survivors, purposeful weight loss may indeed be a key factor for overall physical functioning and advanced lower extremity function • Weight loss and physical activity change interventions can successfully influence functioning despite the underlying symptom severity of overweight survivors 	
Research Gaps: <ul style="list-style-type: none"> • Targeting older survivors, as opposed to excluding, for functional improvement and purposeful weight loss when needed will require innovative intervention approaches to deal with complex illness burden associated with aging • Future studies should determine whether symptom alleviation actually result in improvement in physical function, as is suggested in our preliminary study, and identify which symptoms are critical barriers to function 	

Morey, MC, Snyder, DC, Sloane, R, et al. (2009). Effects of home-based diet and exercise on functional outcomes among older, overweight long-term cancer survivors: RENEW: a randomized controlled trial. *Jama* 301: 1883-1891.

Abstract: CONTEXT: Five-year survival rates for early stage colorectal, breast, and prostate cancer currently exceed 90% and are increasing. Cancer survivors are at greater risk for second malignancies, other comorbidities, and accelerated functional decline. Lifestyle interventions may provide benefit, but it is unknown whether long-term cancer survivors can modify their lifestyle behaviors sufficiently to improve functional status. OBJECTIVE: To determine whether a telephone counseling and mailed print material-based diet and exercise intervention is effective in reorienting functional decline in older, overweight cancer survivors. DESIGN, SETTING, AND PARTICIPANTS: Randomized controlled trial of 641 overweight (body mass index ≥ 25 and < 40), long-term (> 5 years) survivors (aged 65-91 years) of colorectal, breast, and prostate cancer, who were randomly assigned to an intervention group (n = 319) or delayed intervention (control) group (n = 322) in Canada, the United Kingdom, and 21 US states. Individuals were recruited for the Reach out to Enhance Wellness (RENEW) trial from July 1, 2005, through May 17, 2007. INTERVENTION: A 12-month, home-based tailored program of telephone counseling and mailed materials promoting exercise, improved diet quality, and modest weight loss. The control group was wait-listed for 12 months. MAIN OUTCOME MEASURES: Change in self-reported physical function on the Short-Form 36 physical function subscale (score range, 0-100; a high score indicates better functioning) from baseline to 12 months was the primary end point. Secondary outcomes included changes in function on the basic and advanced lower extremity function subscales of the Late Life Function and Disability Index (score range, 0-100), physical activity, body mass index, and overall health-related quality of life. RESULTS: The mean baseline Short-Form 36 physical function score was 75.7. At the 12-month follow-up, the mean function scores declined less rapidly in the intervention group (-2.15; 95% confidence interval [CI], -0.36 to -3.93) compared with the control group (-4.84; 95% CI, -3.04 to -6.63) (P = .03). The mean baseline basic lower extremity function score was 78.2. The mean changes in basic lower extremity function were 0.34 (95% CI, -0.84 to 1.52) in the intervention group compared with -1.89 (95% CI, -0.70 to -3.09) in the control group (P = .005). Physical activity, dietary behaviors, and overall quality of life increased significantly in the intervention group compared with the control group, and weight loss also was greater (2.06 kg [95% CI, 1.69 to 2.43 kg] vs 0.92 kg [95% CI, 0.51 to 1.33 kg], respectively; P < .001). CONCLUSION: Among older, long-term survivors of colorectal, breast, and prostate cancer, a diet and exercise intervention reduced the rate of self-reported functional decline compared with no intervention. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00303875.

Publication Year: 2009	Addresses Premature Aging Specifically:
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Target Population: •Breast, prostate, and colorectal cancer survivors, diagnosed at least 5 years ago , 65 years or older with no evidence of progressive disease or second cancers, •Overweight (BMI ≥ 25)	Type of Intervention: Multicomponent
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Description of Intervention: Diet and exercise intervention: The Reach-Out to Enhance Wellness (RENEW) trial, 12-month home-based diet-exercise intervention

- Tailored mailed-print materials: a personally tailored workbook (the introductory pages featured bar graphs comparing participants' current lifestyle behaviors and weight status with recommended levels, followed by exercise and diet recommendations). A series of quarterly newsletters
- Telephone counseling: Provided to help survivors overcome barriers to change and monitor change; telephone counseling and automated prompts (i.e., 15 sessions and 8 prompts over the 12-month period)

Long Term Cancer Effect Addressed: •Physical Function: change in functional status between baseline and 12 months, was assessed using the physical function subscale of the SF-36

- Lower extremity function: basic and advanced lower extremity function subscales of the Late Life Function and Disability Index
- Other outcomes: target behaviors of physical activity, diet, and weight loss

Summary of Main Points: •The major finding of this trial is that older, overweight long-term cancer survivors successfully engaged in a behavioral lifestyle intervention that resulted in an amelioration of functional decline (reduced the rate of self-reported physical function decline in comparison with a group receiving no intervention)

- This is the first report of a long-term (i.e., 12- month) intervention directed at maintaining function in long-term cancer survivors
- Although the changes observed within the 2 study groups were modest, participants in the intervention group also maintained their lower extremity function whereas participants in the control group experienced a decline
- This home-based strength training intervention provided only moderate to-low doses, and yet was still able to preserve lower extremity functioning

Research Gaps: •Future efforts should be directed toward health promotion programs among older cancer survivors, not only in those who are well beyond their diagnosis, but also in those who are more newly diagnosed and perhaps more motivated to participate in clinical trials targeting lifestyle change

- Studies also should address whether overweight older adults with other conditions might benefit from similar interventions, especially given the current paradoxical controversy over weight loss as beneficial or detrimental in overweight older adults
- Future studies should not only assess the effect on health and well-being, but also should address cost-related outcomes, especially given that the economic burden associated with functional decline and loss of independence is exceedingly high

Pakiz, B, Flatt, SW, Bardwell, WA, et al. (2011). Effects of a weight loss intervention on body mass, fitness, and inflammatory biomarkers in overweight or obese breast cancer survivors. International journal of behavioral medicine 18: 333-341.

Abstract: BACKGROUND: Obesity is characterized by chronic mild inflammation and may influence the risk and progression of cancer. PURPOSE: The current study is an exploratory analysis of the effect of a weight loss intervention that emphasized increased physical activity on inflammatory cytokines (tumor necrosis factor-alpha [TNF-alpha], interleukin-6 [IL-6], interleukin-8 [IL-8], and vascular endothelial growth factor [VEGF]) at the end of the 16-week intervention period in overweight breast cancer survivors. METHODS: Study participants averaged 56 years of age (N=68). Intervention participants (n=44 vs. 24 controls) participated in a cognitive behavioral therapy-based weight management program as part of an exploratory randomized trial. The intervention incorporated strategies to promote increased physical activity and diet modification. Baseline and 16-week data included height, weight, body composition, physical activity level, and biomarkers IL-6, IL-8, TNF-alpha, and VEGF. RESULTS: Weight loss was significantly greater in the intervention group than controls (-5.7 [3.5] vs. 0.2 [4.1] kg, P<0.001). Paired t tests noted favorable changes in physical activity level (P<0.001 intervention, P=0.70 control), marginally lower IL-6 levels (P=0.06 intervention, P=0.25 control) at 16 weeks for participants in the intervention group, and lower TNF-alpha levels for participants in the intervention (P<0.05) and control groups (P<0.001). Increased physical activity was associated with favorable changes in IL-6 for participants in the intervention group (R(2) =0.18; P<0.03). CONCLUSION: Favorable changes in cytokine levels were observed in association with weight loss in this exploratory study with overweight breast cancer survivors.

Publication Year: 2011	Addresses Premature Aging Specifically: No
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Target Population: Overweight breast cancer survivors	Type of Intervention: Multicomponent
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Description of Intervention: Cognitive behavioral therapy (CBT) intervention for weight loss through exercise and diet modification:

- 16-week intervention
- Participants attended group sessions and were advised to self-monitor with food diaries and exercise logs
- Telephone contact was made 4 times in the initial 2 weeks and once weekly following this period
- Physical activity (PA) component: encouraged regular planned aerobic exercise (initial goal of daily activity and a step-wise increase in time and intensity) and the overall long-term goal being an average of 1 h per day of moderate to vigorous PA
- Muscle strengthening exercises were demonstrated, practiced, and encouraged during group sessions, with the goal of performing this activity 2–3 times per week -A pedometer was provided
- Dietary guidance promoted negative energy balance through energy restriction and increased energy expenditure. A deficit of 500–1,000 kcal/day was the goal, particularly via reduced energy density of the diet, plus avoidance of overly strict dieting behavior that did not promote satiety or long-term maintenance

Long Term Cancer Effect Addressed:

- Body composition: Whole body and regional body fat, lean soft tissue mass, and percent fat were obtained from total body DXA scans
- Other outcomes: anthropometry, PA level, lipid profile

Summary of Main Points:

- Results from the present study reports indicate that 16 weeks of involvement in a behavioral program to promote weight management through exercise and diet modification is effective in reducing selected risk factors for CVD
- Participants in the weight management intervention group lost a significant amount of weight and fat mass while maintaining lean tissue mass. Importantly, the average BMI category decreased from ‘obese’ to ‘overweight’ in the intervention group, and their group mean waist circumference decreased below the gender-neutral threshold for obesity risk
- Blood lipid profiles were improved among women in the intervention group. Importantly, after participating in the intervention program, these women were able to lower their TC to a level no longer at risk for CVD

Research Gaps: Long-term studies are needed to determine the effects of behavioral interventions on recurrence of the disease and Survival

Travier, N, Buckland, G, Vendrell, JJ, et al. (2018). Changes in metabolic risk, insulin resistance, leptin and adiponectin following a lifestyle intervention in overweight and obese breast cancer survivors. European journal of cancer care 27: e12861.

Abstract: Adiposity and physical activity are modifiable factors that could be important determinants of breast cancer (BC) prognosis through their effects on endogenous reproductive hormones, chronic inflammation and metabolic changes. Therefore, it is necessary to evaluate whether offering lifestyle interventions to BC survivors could affect the levels of certain biomarkers involved in these mechanisms. We designed a pre-post intervention study offering diet and exercise sessions over 12 weeks to 42 overweight/obese BC survivors. Before and after the intervention, we obtained dietary information, anthropometry and cardiorespiratory fitness (CRF) measurements and blood samples to measure metabolic risk, insulin resistance and adipokines biomarkers. Wilcoxon signed-rank tests and Spearman partial correlation coefficients were used to compare pre- and post-measurements and assess the correlations between changes in biomarkers and changes in anthropometry and CRF. Breast cancer survivors showed significant improvements in metabolic risk biomarkers and insulin resistance indicators along with a non-significant leptin decrease and a significant adiponectin decrease. The improvements in metabolic risk biomarkers, insulin resistance indicators and leptin were moderately correlated ($0.32 \leq |r| \leq 0.55$) with the decrease in body mass index and the increase in CRF. Diet and exercise interventions implemented in overweight/obese BC survivors may improve metabolic risk, insulin resistance and leptin biomarkers.

Publication Year: 2018	Addresses Premature Aging Specifically: No
Target Population: Overweight/obese breast cancer (BC) survivors	Type of Intervention: Multicomponent
<p>Description of Intervention: Lifestyle diet and exercise intervention: 12-week intervention</p> <ul style="list-style-type: none"> •Dietary component: 12 weekly 1-hr group sessions led by a trained dietician -Included theoretical content (e.g., food groups, the food pyramid, healthy choices, cooking, weekly menus) and group discussion focusing on the weight loss goals and achievements of each participant •Exercise component: 24 bi-weekly sessions (75 min each) of aerobic and muscle strengthening exercises, led by trained PA monitors 	
<p>Long Term Cancer Effect Addressed: •Cardiorespiratory fitness (CRF)</p> <ul style="list-style-type: none"> • Measurements and blood samples to measure metabolic risk, insulin resistance and adipokines biomarkers •Dietary information, anthropometry 	
<p>Summary of Main Points: •Diet and exercise interventions implemented in overweight/obese BC survivors may improve metabolic risk, insulin resistance and leptin biomarkers</p> <ul style="list-style-type: none"> •Breast cancer survivors showed significant improvements in metabolic risk biomarkers and insulin resistance indicators along with a non-significant leptin decrease and a significant adiponectin decrease •The improvements in metabolic risk biomarkers, insulin resistance indicators and leptin were moderately correlated with the decrease in body mass index and the increase in CRF 	
<p>Research Gaps: •Large long-term controlled trials, offering cost-effective interventions combining exercise and diet to BC survivors early after treatment are needed to evaluate whether the beneficial short-term effects of these interventions could lead to long-term effects involving reductions in common comorbidities in BC survivors such as hypertension, coronary heart disease, stroke and diabetes, as well as decreases in BC recurrence and increase in survival</p>	

Winger, JG, Mosher, CE, Rand, KL, et al. (2014). Diet and exercise intervention adherence and health-related outcomes among older long-term breast, prostate, and colorectal cancer survivors. Annals of behavioral medicine: a publication of the Society of Behavioral Medicine 48: 235-245.

Abstract: BACKGROUND: Diet and exercise interventions for cancer survivors result in health benefits; however, few studies have examined health outcomes in relation to adherence. PURPOSE: We examined associations between adherence to components of a diet-exercise intervention and survivors' physical and mental health. METHODS: A randomized controlled trial tested a telephone and mailed print intervention among 641 older, overweight, long-term survivors of breast, prostate, and colorectal cancer. Dietary and exercise behaviors were assessed at 14 time points throughout the year-long intervention; health outcomes were examined postintervention. RESULTS: Telephone session attendance had significant indirect relationships with health outcomes through intervention-period exercise and dietary behavior. Attendance showed positive indirect relationships with physical function (beta = 0.11, p < 0.05), basic and advanced lower extremity function (beta = 0.10, p < 0.05/beta = 0.09, p < 0.05), and mental health (beta = 0.05, p < 0.05), and a negative indirect relationship with body mass index (beta = -0.06, p < 0.05). CONCLUSIONS: Session attendance is vital in facilitating improvement in health behaviors and attendant outcomes (Clinicaltrials.gov number NCT00303875).

Publication Year: 2014	Addresses Premature Aging Specifically: Yes
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Target Population: Older, overweight, long-term survivors of breast, prostate, and colorectal cancer	Type of Intervention: Multicomponent
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Description of Intervention: Diet and exercise intervention: The Reach-Out to Enhance Wellness (RENEW) trial, 12-month home-based diet-exercise intervention

- Tailored mailed-print materials: a personally tailored workbook (the introductory pages featured bar graphs comparing participants' current lifestyle behaviors and weight status with recommended levels, followed by exercise and diet recommendations). A series of quarterly newsletters
- Telephone counseling: Provided to help survivors overcome barriers to change and monitor change; telephone counseling and automated prompts (i.e., 15 sessions and 8 prompts over the 12-month period)

*This paper on RENEW intervention assesses the relationship between adherence to the intervention and the outcomes

Long Term Cancer Effect Addressed:

- Physical Function: change in functional status between baseline and 12 months, was assessed using the physical function subscale of the SF-36
- Lower extremity function: lower extremity function subscales of the Late Life Function and Disability Index
- Mental health: 14-item mental health summary measure of the Medical Outcomes Study SF-36. The mental health measure is an aggregate of 4 subscales: (a) vitality, (b) social functioning, (c) role limitations due to emotional problems, and (d) general mental health (i.e., depression and anxiety)

Summary of Main Points:

- Increases in some health behaviors (i.e., strength and endurance exercise and fruit and vegetable intake) over the intervention period accounted for the relationship between increased telephone session attendance and certain health benefits
- These findings support the importance of targeting social cognitive theory-based determinants of behavior change in health promotion interventions
- Endurance exercise was positively related to physical function and basic and advanced lower extremity function and negatively related to body mass index
- Increased strength exercise was related to improved mental health

Research Gaps:

- Participants were predominately White and represented a minority of those approached to participate in the study. Thus, findings warrant replication in samples that are representative of the general population of older, overweight, long-term cancer survivors
- Future studies should consider investigating strategies to increase session attendance (e.g., flexible telephone counseling session schedules, incentives for session attendance, or improved staff training)
- Future intervention trials could implement a dose-response design testing the relationship between varying doses of the intervention (e.g., number of counseling sessions) and outcomes

Multicomponent Interventions

Reviews

Pekmezi, DW, Demark-Wahnefried, W. (2011). Updated evidence in support of diet and exercise interventions in cancer survivors. Acta oncologica (Stockholm, Sweden) 50: 167-178.	
Publication Year: 2011	Type of Review: Narrative Review
<p>Abstract: BACKGROUND: A growing body of evidence suggests that diet and exercise behaviors and body weight status influence health-related outcomes after a cancer diagnosis. This review synthesizes the recent progress in lifestyle interventions in light of current guidelines put forth by the American Cancer Society (ACS), the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) and the American College of Sports Medicine (ACSM). METHODS: The PubMed database was searched for terms of cancer survivor(s) or neoplasms/survivor, cross-referenced with MeSH terms of lifestyle, health behavior, physical activity, exercise, body weight, obesity, weight loss, diet, nutrition, and intervention studies and limited to randomized controlled trials (RCTs) that had retention rates exceeding 75%. RESULTS: There has been an increase in the number and methodological rigor of the studies in this area, with 21 RCTs identified in the past three years. Results suggest that physical activity interventions are safe for cancer survivors and produce improvements in fitness, strength, physical function, and cancer-related psychosocial variables, whereas dietary interventions improve diet quality, nutrition-related biomarkers and body weight. Preliminary evidence also suggests that diet and exercise may positively influence biomarkers associated with progressive disease and overall survival (e.g., insulin levels, oxidative DNA damage, tumor proliferation rates). DISCUSSION: The evidence base regarding health-related benefits of increased physical activity, an improved diet, and weight control continues to expand. Due to the large (and increasing) number of cancer survivors, more research is needed that tests the impact of lifestyle change on health-related outcomes in this population, especially research that focuses on high-reach, sustainable interventions that recruit diverse, representative samples to help increase the generalizability of findings to the population at large. Concurrent research also needs to address relative benefit in relation to various subpopulations as defined by phenotype, genotype, and/or exposures to treatment, and other lifestyle and environmental factors.</p>	
Addresses Premature Aging Specifically: No	Target Population: Cancer survivors
Type of Intervention: Multicomponent	
Description of Intervention: Lifestyle (Diet and Physical Activity): interventions that promote improvements in diet (e.g., low fat diet, increased consumption of fruits and vegetables, or dietary supplementation such as flax seed consumption) and/or exercise behaviors (supervised exercise or walking programs, yoga, resistance training) some are multicomponent and incorporate both)	
<p>Long Term Cancer Effect Addressed:</p> <ul style="list-style-type: none"> •Fitness outcomes •Psychosocial outcomes •Health behaviors (e.g., diet) 	
<p>Summary of Main Points:</p> <ul style="list-style-type: none"> •The number of randomized trials testing lifestyle interventions in cancer survivors is growing, but the evidence base is still limited •This review uncovered more published studies on physical activity interventions for cancer survivors, than those involving dietary modification •Lifestyle interventions for cancer survivors appear to still focus on outcomes related to fitness, diet, and cancer-related psychosocial factors •Physical activity interventions were shown to be safe for cancer survivors and produce improvements in fitness, strength, and quality of life (e.g., fatigue) •Dietary interventions found significant improvements in diet quality, restriction of dietary fat, and increased fruit and vegetable consumption (as well as serum markers associated with these foods) 	
<p>Research Gaps:</p> <ul style="list-style-type: none"> •Most available studies recruited primarily White samples, including other racial/ethnic groups in future trials would help increase the generalizability of such findings to the population at large •Despite advocacy of multi-component lifestyle interventions, there still are relatively few studies of combined programs for cancer survivors 	

- RCTs testing the effects of physical activity and diet on survival have been called for in prior reviews and are still needed. Such studies would provide critical information about whether and how much lifestyle change can affect prognosis
- Future research should focus on developing and testing interventions with potential for sustainability and disseminability in order to serve the growing population of cancer survivors

Reeves, MM, Terranova, CO, Eakin, EG, et al. (2014). Weight loss intervention trials in women with breast cancer: a systematic review. Obesity reviews: an official journal of the International Association for the Study of Obesity 15: 749-768.

Publication Year: 2014	Type of Review: Systematic Review
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Abstract: Obesity has been associated with poor health outcomes in breast cancer survivors. Thus, weight loss is recommended for overweight and obese survivors. We systematically reviewed studies (published up to July 2013) that evaluated behaviourally based, weight loss interventions in women with breast cancer exclusively. Completed randomized trials, single-arm trials and ongoing trials were reviewed. Within-group and between-group differences for weight loss were extracted, as was data on secondary outcomes, i.e. clinical biomarkers, patient-reported outcomes, adverse events. Ten completed randomized trials, four single-arm trials and five ongoing trials were identified. Statistically significant within-group weight loss was observed over periods of 2 to 18 months in 13 of the 14 trials, with six randomized and two single-arm trials observing mean weight loss $\geq 5\%$. Clinical biomarkers, psychosocial and patient-reported outcomes were measured in a small number of studies. No serious adverse events were reported. Only two trials assessed maintenance of intervention effects after the end-of-intervention and none reported on cost-effectiveness. The studies included in this review suggest that weight loss is feasible to achieve and is safe in women following treatment for breast cancer. Future studies should assess (and be powered for) a range of biomarker and patient-reported outcomes, and be designed to inform translation into practice.

Addresses Premature Aging Specifically: No	Target Population: Women with breast cancer
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Type of Intervention: Multicomponent

Description of Intervention: Behaviorally-based, weight loss interventions:

- The majority of weight loss interventions (6/10 included trials) addressed both diet and PA (4 addressed diet only)

Long Term Cancer Effect Addressed: •Studies have generally focused on weight loss as the primary outcome, with over half also reporting on changes in central obesity (waist circumference)

- However, very few studies have reported on psychosocial and treatment-related outcomes, and with the

Summary of Main Points: •There is a small but growing body of evidence to suggest that weight loss is feasible and safe in women following treatment for breast cancer

- The studies included in this review suggest that weight loss is feasible to achieve and safe in women following treatment for breast cancer

- Longer (>6-months) weight loss interventions and those that addressed a combination of diet, PA and behavior modification tended to achieve greater weight loss

- In women following treatment for breast cancer, intentional weight loss of $\geq 5\%$ was associated with reductions in insulin and leptin of 30-40%. Reductions in CRP were less consistent and changes in other inflammatory markers and adiponectin appeared unrelated to weight loss. This evidence however, is based on a small number of generally underpowered studies

Research Gaps: •Further controlled trials in larger samples are needed to understand the influence of intentional weight loss on cancer-related biomarkers in breast cancer survivors. This research should be conducted alongside the advances in identification of biomarkers most salient to breast cancer

- Future studies should assess (and be powered for) a range of biomarker and patient-reported outcomes, and be designed to inform translation into practice

- Also of particular relevance for breast cancer survivors, is assessment of comorbidity-related outcomes

- Inclusion of a control group, or more specifically an attention-control group, in future trials is important to further inform the extent to which beneficial effects on patient-reported outcomes can be attributed to weight loss versus more generic support/attention

Cognitive Interventions

Original Research

<p>Abrahams, HJG, Gielissen, MFM, Donders, RRT, et al. (2017). The efficacy of Internet-based cognitive behavioral therapy for severely fatigued survivors of breast cancer compared with care as usual: a randomized controlled trial. <i>Cancer</i> 123: 3825-3834.</p>	
<p>Abstract: BACKGROUND: Severe fatigue is a common and distressing symptom affecting approximately one in four survivors of breast cancer. The current study examined the efficacy of Internet-based cognitive behavioral therapy (ICBT) for severe fatigue in survivors of breast cancer compared with care as usual (CAU). METHODS: The authors conducted a parallel-group randomized controlled trial. Severely fatigued, disease-free survivors of breast cancer who had completed cancer treatment at least 3 months previously were eligible. Participants were randomly allocated to ICBT or CAU using computer-generated stratified block randomization. The primary outcome of fatigue severity was assessed at baseline and after 6 months, as were the secondary outcomes of functional impairment, psychological distress, and quality of life. Statistical effects were tested with analyses of covariance (intention-to-treat analysis). RESULTS: Participants were recruited between January 2014 and March 2016 and assigned to ICBT (66 patients) or CAU (66 patients). Compared with the participants who had received CAU, those who had received ICBT reported lower fatigue scores at 6 months (mean difference [Delta], 11.5; 95% confidence interval [95% CI], 7.7-15.3) and a large effect size (Cohen d = 1.0), with the majority of patients (73%) demonstrating clinically significant improvement. ICBT also was found to lead to lower functional impairment (Delta, 297.8; 95% CI, 145.5-450.1) and psychological distress scores (Delta, 5.7; 95% CI, 3.4-7.9) and higher quality-of-life scores (Delta, 11.7; 95% CI, 5.8-17.7) compared with CAU, with medium to large effect sizes (Cohen d = 0.6-0.8). CONCLUSIONS: ICBT appears to be effective in reducing severe fatigue and related symptoms and meets the current need for easy accessible and more efficient evidence-based treatment options for severely fatigued survivors of breast cancer. <i>Cancer</i> 2017;123:3825-34. (c) 2017 American Cancer Society.</p>	
<p>Publication Year: 2017</p>	<p>Addresses Premature Aging Specifically: No</p>
<p>Target Population: Fatigued survivors of breast cancer</p>	<p>Type of Intervention: Cognitive</p>
<p>Description of Intervention: Internet-based cognitive behavioral therapy (IBCBT):</p> <ul style="list-style-type: none"> •3 face-to-face sessions and a maximum of 8 web-based modules, guided by licensed cognitive behavioral therapists through electronic consultations (i.e., E-mail contacts and a maximum of 2 telephone or video consultations), tailored to the individual patient •The intended duration of ICBT was 6 months •The protocol is based on a cognitive behavioral model of precipitating and perpetuating factors of fatigue, in which it is assumed that the malignancy and its treatment induce the fatigue whereas cognitive behavioral factors (e.g., a deregulated sleep-wake cycle or dysfunctional cognitions regarding fatigue) maintain the fatigue 	
<p>Long Term Cancer Effect Addressed:</p> <ul style="list-style-type: none"> •Functional impairment: assessed with the Sickness Impact Profile 8 •Psychological distress: assessed with the Brief Symptom Inventory 18 •Fatigue severity: assessed with the 8-item CIS-Fatigue Severity 	
<p>Summary of Main Points:</p> <ul style="list-style-type: none"> •Participants in the ICBT condition reported significantly less fatigue, with a large effect size and the majority demonstrating clinically significant and self-rated improvement •ICBT also was found to lead to significantly less functional impairment and psychological distress and a better QOL 	
<p>Research Gaps:</p> <ul style="list-style-type: none"> •The participants in the current study were relatively young, whereas breast cancer is most prevalent among women aged 60 to 75 years. This limits the generalizability of the current study results and may indicate that ICBT in particular attracts younger women, but we must not overlook those severely fatigued survivors of breast cancer whose Internet literacy skills are deficient or who reject online interventions •The current study should be replicated among cancer survivors with different tumor types because we are unsure whether the results of the current study can be generalized to these patient populations 	

Alvarez, J, Meyer, FL, Granoff, DL, et al. (2013). The effect of EEG biofeedback on reducing postcancer cognitive impairment. Integrative cancer therapies 12: 475-487.

Abstract: UNLABELLED: BACKGROUND AND HYPOTHESES: Postcancer cognitive impairment (PCCI) is observed in a substantial number of breast cancer survivors, persisting for as long as 20 years in some subgroups. Although compensatory strategies are frequently suggested, no restorative interventions have yet been identified. This study examined the feasibility of EEG biofeedback ("neurofeedback") and its potential effectiveness in reducing PCCI as well as the fatigue, sleep disturbance, and psychological symptoms that frequently accompany PCCI. STUDY DESIGN: This was a 6-month prospective study with a waitlist control period followed by an active intervention. Participants were female breast cancer survivors (n = 23), 6 to 60 months postchemotherapy, with self-reported cognitive impairment. METHODS: Four self-report outcome measures (Functional Assessment of Cancer Therapy-Cognitive Function [FACT-Cog], Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-Fatigue], Pittsburgh Sleep Quality Index [PSQI], and Brief Symptom Inventory [BSI]-18) were administered 3 times during a 10-week waitlist control period, 3 times during a 10-week (20-session) neurofeedback training regimen, and once at 4 weeks postneurofeedback. RESULTS: All 23 participants completed the study, demonstrating the feasibility of EEG biofeedback in this population. Initially, the sample demonstrated significant dysfunction on all measures compared with general population norms. Repeated-measures ANOVAs revealed strongly significant improvements ($P < .001$) on all 4 cognitive measures (perceived cognitive impairment, comments from others, perceived cognitive abilities, and impact on quality of life [QOL]), the fatigue scale, and the 4 psychological scales (somatization, depression, anxiety and global severity index) as well as on 3 of 8 sleep scales (quality, daytime dysfunction, and global). Two of the other sleep scales (latency and disturbance) were significant at $P < .01$, and 1 (use of medication) at $P < .05$; 2 were not significant. Improvements were generally linear across the course of training, and were maintained at the follow-up testing. At the follow-up testing, the sample no longer differed significantly from normative populations on 3 of the 4 FACT-Cog measures (impairment, impact on QOL, and comments), FACIT-Fatigue, PSQI sleep quality and habitual efficiency, or any of the BSI-18 measures of psychological disturbance. CONCLUSIONS: Data from this limited study suggest that EEG biofeedback has potential for reducing the negative cognitive and emotional sequelae of cancer treatment as well as improving fatigue and sleep patterns.

Publication Year: 2013	Addresses Premature Aging Specifically: No
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Target Population: Female breast cancer survivor, age 40 years or older, 6-60 months post chemotherapy, self-reported cognitive impairment since cancer diagnosis or treatment	Type of Intervention: Cognitive
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Description of Intervention: EEG biofeedback (neurofeedback): a real-time display of the brain's electrical activity, fed back as visual or auditory information, enables the user to modify that brainwave activity

- The present study used a newer approach to neurofeedback, rooted in the global view of brain function: the NeuroOptimal system, designed to train the brain as a whole, without reference to particular locations or frequencies. Unlike classical neurofeedback approaches, the participant in the Zengar approach simply "lets go" and allows the brain to use the feedback—provided as brief interruptions to the music he or she is hearing—to enable its own innate capacity for self-organization
- Neurofeedback was administered twice a week—in most cases, at the same time of day—for 10 weeks, using the Zengar

Long Term Cancer Effect Addressed:

- Cognitive Function: Functional Assessment of Cancer Therapy–Cognitive Function (FACT-Cog)
- Other outcomes: sleep quality, fatigue, QoL, depression, and anxiety

Summary of Main Points:

- Breast cancer survivors demonstrated significant baseline impairments in self-reported cognitive function, fatigue, sleep quality, and psychological well-being as compared with a normal population. After 10 weeks (20 sessions) of neurofeedback, their performance in these areas had improved to levels indistinguishable from population norms
- Participants were continuing to improve on most measures through the end of the training period. Therefore, it is possible that a longer period of neurofeedback training would have resulted in even greater improvement

Research Gaps: •EEG biofeedback deserves further study as a novel method of addressing post cancer cognitive impairment (PCCI) that may be safe, effective, and acceptable to patients

- The positive results obtained through this form of neurofeedback nonetheless suggest that further study of this intervention for PCCI is warranted. In a future study, we hope to include both neuropsychological assessment and fMRI scans before and after the neurofeedback regimen to identify more precisely the nature of the changes occurring
- A study of neurofeedback delivered during cancer treatment would help determine whether the incidence and/or severity of PCCI can be reduced through this intervention
- To establish whether or not the training itself is truly causal, a double-blind, fully controlled study, including an active control group receiving sham neurofeedback, should be undertaken

Becker, H, Henneghan, AM, Volker, DL, et al. (2017). A Pilot Study of a Cognitive-Behavioral Intervention for Breast Cancer Survivors. Oncology nursing forum 44: 255-264.

Abstract: PURPOSE/OBJECTIVES: To test combining a group intervention to build self-efficacy for using compensatory strategies and lifestyle adjustments with brain-training practice to improve cognition.. DESIGN: A quasiexperimental design.. SETTING: Texas Oncology, a community oncology practice in Austin.. SAMPLE: 20 women aged 35-65 years, who had finished chemotherapy at least three months before the study, were within five years of completing all treatment, and had self-reported cognitive concerns. . METHODS: Six group sessions to build self-efficacy for using compensatory strategies, along with other health behaviors that affect cognitive performance, were combined with practice on a computer-based training program. Female breast cancer survivors were recruited through flyers, mailings, and personal contacts. . MAIN RESEARCH VARIABLES: Cognitive performance, cognitive concerns, cognitive/memory strategies, fatigue, emotional distress, sleep disorders, and quality of life.. FINDINGS: Participants reported that the intervention was useful in building cognitive abilities. Although scores on performance tests did not increase, ratings of cognitive concerns, fatigue, emotional distress, and sleep disturbance decreased significantly. Use of cognitive/memory strategies increased significantly. . CONCLUSIONS: This pilot study demonstrated the feasibility of combining a group intervention with brain-training practice. A larger randomized trial would afford a more rigorous test of efficacy.. IMPLICATIONS FOR NURSING: A growing body of evidence regarding potential interventions to address survivors' cognitive problems exists. Nurses should counsel breast cancer survivors about fatigue, sleep deprivation, and emotional distress, as well as the effects of cancer treatment on cognition.

Publication Year: 2017	Addresses Premature Aging Specifically: No
Target Population: Women, age 35–65 years, ≥ 3 months ≤ 5 years post chemotherapy, self-reporting cognitive dysfunction	Type of Intervention: Cognitive

Description of Intervention: Computer-based brain-training program: group sessions combined with practice

- Group sessions: six 90-minutes group sessions facilitated by a master’s-prepared nurse to build self-efficacy for using compensatory strategies, along with other health behaviors that affect cognitive performance. Theory-driven, informed by Pender’s (1987) model of health promotion and Bandura’s (1989) social cognitive theory
- BrainHQ computer-based training program: BrainHQ targets a broad range of cognitive domains. Each week, participants were assigned a different set of cognitive exercises covering the domains of attention, memory, brain speed, people (recognition) skills, navigation, and intelligence. They were asked to practice the exercises for 45 minutes three to four times per week

Long Term Cancer Effect Addressed: •Cognitive function:

- The California Verbal Learning Test®(CVLT) assesses verbal learning and remembering
- The Controlled Oral Word Association Test (COWAT) is a speed test of verbal fluency and word finding
- The Symbol Digit Modalities Test (SDMT) assesses complex scanning and tracking
- The 30-item Everyday Problems Test–Revised to assess the ability to reason and solve everyday problems

Summary of Main Points: •This small pilot study demonstrated the feasibility of combining a group intervention focused on building self-efficacy for using compensatory strategies and lifestyle adjustments with brain-training practice

- Behavioral interventions, such as the one piloted in this study, can have positive effects on survivors’ self-reported cognitive abilities, fatigue, sleep disturbance, and emotional distress, as well as their use of cognitive and memory strategies

Research Gaps: •Future research should explore alternative methods of delivering a cognitive intervention (since this intervention demanded time and energy, both of which may be in short supply for cancer survivors, particularly those who are trying to continue to work). One alternative might be to combine fewer face-to-face classes with telephone or video conferencing or to explore Internet-based options

- Although cognitive test performance did not improve following the intervention, positive changes were seen in women’s self-reports of cognitive concerns and symptoms that can affect cognitive functioning (e.g., fatigue, sleep disturbance, emotional distress)
- Although this intervention was well received, future studies should investigate alternative methods for building cognitive abilities among survivors who are unable or not interested in participating in group interventions

Meneses, K, Benz, R, Bail, JR, et al. (2018). Speed of processing training in middle-aged and older breast cancer survivors (SOAR): results of a randomized controlled pilot. Breast cancer research and treatment 168: 259-267.	
Abstract: PURPOSE: Cognitive changes are common among breast cancer survivors. There is limited evidence to guide management of cognitive changes. This randomized controlled pilot evaluated the preliminary efficacy of a speed of processing (SOP) training among middle-aged and older breast cancer survivors. METHODS: Sixty breast cancer survivors with self-reported cognitive changes were recruited to the SOAR study. Participants were randomized to either a home-based SOP training (n = 30) or no-contact control group (n = 30). Primary outcomes were SOP (Useful Field of View Test((R))), and executive function (NIH Toolbox Cognition Battery). Neuropsychological assessments were completed at baseline, 6 weeks, and 6 months post study entry. Data were analyzed using repeated measures t tests, analysis of covariance, and sensitivity analyses. RESULTS: SOP training resulted in improvement in objective measures of SOP and executive function. Immediate (6 week) posttest and 6-month follow-up demonstrated large SOP training effects over time. Large representation of African American women (51.2%) and 96% retention in the SOAR study add to study strengths. CONCLUSION: Home-based SOP training shows promise for remediating cognitive changes following breast cancer treatment, particularly improved SOP, and executive function.	
Publication Year: 2018	Addresses Premature Aging Specifically: No
Target Population: Adults with breast cancer diagnosis, ≥ 6 months post primary breast cancer treatment	Type of Intervention: Cognitive
Description of Intervention: Home-based Speed of Processing (SOP) training: The Speed of Processing in Middle-Aged and Older Breast Cancer Survivors (SOAR) Study: <ul style="list-style-type: none"> •The SOP training accessed by participants from their personal computers at home •The SOP training used the commercially available “Double Decision” program which involves identifying a central target (either a car or a truck) and noticing where a peripheral target was located in conditions with varying degrees of difficulty (i.e., increased distractors in the periphery or the addition of another central target). The exercises automatically adjust to user performance to maintain a 75% correct rate during the training session in order to promote motivation •Participants in the intervention group were instructed to complete 2 h of SOP training per week for a total of 10 h within 6–8 weeks •Participants also received weekly contact via their preferred method (i.e., telephone call, text, or email) to remind them about their SOP training 	
Long Term Cancer Effect Addressed: <ul style="list-style-type: none"> •Cognitive Function, executive function, episodic memory (NIH Toolbox Cognition Battery (NIHTB-CB) •SOP (Useful field of view (UFOV®) test 	
Summary of Main Points: <ul style="list-style-type: none"> •The intervention condition improved on six cognitive outcomes on post-test 1(6-week) and on 7 outcomes on post-test 2 (6-month) •These training gains can occur when the SOP training is completed in the participants’ home rather than in a research laboratory setting 	
Research Gaps: <ul style="list-style-type: none"> •Future research should also consider dosage as an important component of therapeutic benefit •Future studies of SOP with breast cancer survivors should consider other effects that have been found in other populations including: driving ability, depression, self-rated health, health-related quality of life, and locus of control 	

Prinsloo, S, Novy, D, Driver, L, et al. (2017). Randomized controlled trial of neurofeedback on chemotherapy-induced peripheral neuropathy: a pilot study. Cancer 123: 1989-1997.

Abstract: BACKGROUND: Chemotherapy-induced peripheral neuropathy (CIPN) is a significant problem for cancer patients, and there are limited treatment options for this often debilitating condition. Neuromodulatory interventions could be a novel modality for patients trying to manage CIPN symptoms; however, they are not yet the standard of care. This study examined whether electroencephalogram (EEG) neurofeedback (NFB) could alleviate CIPN symptoms in survivors. METHODS: This was a randomized controlled trial with survivors assigned to an NFB group or a wait-list control (WLC) group. The NFB group underwent 20 sessions of NFB, in which visual and auditory rewards were given for voluntary changes in EEGs. The Brief Pain Inventory (BPI) worst-pain item was the primary outcome. The BPI, the Pain Quality Assessment Scale, and EEGs were collected before NFB and again after treatment. Outcomes were assessed with general linear modeling. RESULTS: Cancer survivors with CIPN (average duration of symptoms, 25.3 mo), who were mostly female and had a mean age of 62.5 years, were recruited between April 2011 and September 2014. One hundred percent of the participants starting the NFB program completed it (30 in the NFB group and 32 in the WLC group). The NFB group demonstrated greater improvement than the controls on the BPI worst-pain item (mean change score, -2.43 [95% confidence interval, -3.58 to -1.28] vs 0.09 [95% confidence interval, -0.72 to -0.90]; P =.001; effect size, 0.83). CONCLUSIONS: NFB appears to be effective at reducing CIPN symptoms. There was evidence of neurological changes in the cortical location and in the bandwidth targeted by the intervention, and changes in EEG activity were predictive of symptom reduction.

Publication Year: 2017

Addresses Premature Aging Specifically: No

Target Population: Participants with any type or stage of cancer; with at least a grade 3 neuropathy rating according to the NCI's grading criteria and/or reported Chemotherapy-induced peripheral neuropathy (CIPN)-related moderate to severe pain, and had symptoms of neurop

Type of Intervention: Cognitive

Description of Intervention: Electroencephalogram (EEG) neurofeedback (NFB): NFB takes advantage of the learning process by providing feedback to the participant about the workings of his or her own brain in real time

- 20 sessions of NFB over a maximum of 10 weeks; minimum participation of twice weekly
- Sensors are placed on the participant's scalp at appropriate locations
- Participants choose a game that rewards them for changing their brainwave activity under the sensors
- Feedback is both auditory and visual (an emotionally neutral picture appears on the screen and is accompanied by a simultaneous auditory beep when participants successfully modify their brain activity)
- By targeting changes in brain regions that are active during pain conditions such as CIPN, NFB can teach participants to interpret pain signals differently

Long Term Cancer Effect Addressed:

- Pain: the Brief Pain Inventory (BPI)
- CIPN-related symptoms, such as average pain, pain severity, activity interference, and affective interference (BPI) and pain unpleasantness, tingling, numbness, intensity, tenderness, surface pain, and deep pain (measured with the Pain Quality Assessment Scale [PQAS])

Summary of Main Points:

- NFB appears to be an effective symptom-control strategy for survivors suffering from CIPN
- The primary outcome of worst pain, we found had statistically and clinically significant reductions for the NFB group versus the control
- There were also significant improvements in all domains of secondary outcomes, including nonpainful neuropathic symptoms such as numbness and tingling
- This pilot study is the largest clinical trial to determine effects of neuromodulation in cancer survivors

Research Gaps:

- Future research should investigate the efficacy of NFB by chemotherapy type
- An investigation is also needed that includes a sham NFB intervention to elucidate the exact mechanisms of NFB
- Other questions to investigate include the role of NFB in the prevention of CIPN and other cancer pain conditions, the effectiveness of NFB in acute pain settings, and the role of NFB in symptom management both during and after active cancer treatment

Stagl, JM, Bouchard, LC, Lechner, SC, et al. (2015). Long-term psychological benefits of cognitive-behavioral stress management for women with breast cancer: 11-year follow-up of a randomized controlled trial. Cancer 121: 1873-1881.

Abstract: BACKGROUND: Breast cancer survivors experience long-term physical and psychological sequelae after their primary treatment that negatively influence their quality of life (QOL) and increase depressive symptoms. Group-based cognitive-behavioral stress management (CBSM) delivered after surgery for early-stage breast cancer was previously associated with better QOL over a 12-month follow-up and with fewer depressive symptoms up to 5 years after study enrollment. This 8- to 15-year follow-up (median, 11 years) of a previously conducted trial (NCT01422551) evaluated whether women in this cohort receiving CBSM had fewer depressive symptoms and better QOL than controls at an 8- to 15-year follow-up. METHODS: Women with stage 0 to IIIb breast cancer were initially recruited 2 to 10 weeks after surgery and randomized to a 10-week CBSM intervention or a 1-day psychoeducational control group. One hundred women (51 CBSM patients and 49 controls) were recontacted 8 to 15 years after study enrollment to participate in a follow-up assessment. The Center for Epidemiologic Studies-Depression (CES-D) scale and the Functional Assessment of Cancer Therapy-Breast (FACT-B) were self-administered. Multiple regression was employed to evaluate group differences on the CES-D scale and FACT-B over and above effects of confounding variables. RESULTS: Participants assigned to CBSM reported significantly lower depressive symptoms (d, 0.63; 95% confidence interval [CI], 0.56-0.70) and better QOL (d, 0.58; 95% CI, 0.52-0.65) above the effects of the covariates. CONCLUSIONS: Women who received CBSM after surgery for early-stage breast cancer reported lower depressive symptoms and better QOL than the control group up to 15 years later. Early implementation of cognitive-behavioral interventions may influence long-term psychosocial functioning in breast cancer survivors.

Publication Year: 2015	Addresses Premature Aging Specifically: No
Target Population: Women 2–10 weeks post-surgery for non-metastatic Stage 0–IIIb breast cancer	Type of Intervention: Cognitive

Description of Intervention: Cognitive-behavioral stress management CBSM intervention

- 90-min sessions once per week for 10 weeks
- Aimed to improve coping, psychological adaptation, and reduce stress and negative mood using cognitive-behavioral therapy (e.g., cognitive reframing, stress re-appraisal, effective coping skills training, assertiveness training, anger management) and relaxation training (e.g., guided visual imagery, diaphragmatic breathing)

Long Term Cancer Effect Addressed:

- Time to all-cause mortality: days elapsed from date of randomization to death
- Time to breast cancer-specific mortality: days elapsed from date of randomization to breast cancer-related death
- Disease-free interval (local or distant recurrence): was computed as days elapsed from date of randomization to documented breast cancer recurrence

Summary of Main Points:

- Women with Stage 0–IIIb breast cancer who were randomly assigned to a 10-week CBSM intervention 2–10 weeks post-surgery had longer survival, up to 11-years post-enrollment, compared to those in the control group, while accounting for disease- relevant characteristics
- This study provides preliminary evidence that a stress management group intervention modifying psychological adaptation early on in treatment may have lasting effects over the course of the disease for women with breast cancer
- Within the context of a biopsychosocial, multidisciplinary model of care, CBSM is a group-based, manualized, feasible intervention that can be implemented in clinical oncology settings and may provide women an opportunity to reap long-term health benefits in addition to improved QOL and less depressive symptoms

Research Gaps:

- Additional studies should evaluate long-term effects and underlying mechanisms of cognitive-behavioral interventions on clinical disease outcomes of survival and recurrence in non-metastatic breast cancer patients. This is an area in need of further exploration with clinical endpoints as primary outcomes and more rigorous study design
- Research should address whether intervention-related changes in neuroendocrine, immune, inflammatory, and other tumor-promoting processes mediate effects of CBSM on survival
- Future research should also examine whether improved adherence to long-term endocrine regimens or changes in health behaviors may be explanatory mechanisms
- Future research should also investigate the effectiveness of CBSM in venues including oncology clinics and remote platforms, in order to reach the broadest number of patients

Cognitive Interventions

Reviews

Cifu, G, Power, MC, Shomstein, S, et al. (2018). Mindfulness-based interventions and cognitive function among breast cancer survivors: a systematic review. BMC cancer 18: 1163.	
Publication Year: 2018	Type of Review: Systematic Review
<p>Abstract: BACKGROUND: Breast cancer survivors have an elevated risk of cognitive impairment compared to age-matched women without cancer. Causes of this impairment are complex, including both treatment and psychological factors. Mindfulness-based interventions, which have been shown to improve cognitive function in the general population, may be one approach to mitigate cognitive impairment in this survivor population. Our objective was to conduct a systematic literature review of studies on the effect of mindfulness-based interventions on cognition among breast cancer survivors. METHODS: We conducted searches of three electronic databases (Scopus, PubMed and Cochrane Database of Systematic Reviews) in September 2017 for studies pertaining mindfulness and cognitive function among breast cancer survivors. Abstracts were manually searched by two reviewers and additional articles were identified through reference lists. RESULTS: A total of 226 articles were identified through our systematic search and six met inclusion criteria for this review. The reviewed studies lacked consistency in terms of the cognition domains studied (e.g. executive function, recent memory, etc) and in the measures used to assess cognition. Of the included studies, two found no association between mindfulness interventions and cognitive function, two found improvement that was not sustained at the follow-up, and another two found sustained improvement at 2- or 6-months. CONCLUSIONS: Mindfulness-based interventions have shown some evidence for improving cognition among breast cancer survivors, but further research using validated and comprehensive cognitive assessments is needed. More research is also needed related to the timing, duration and content of mindfulness interventions.</p>	
Addresses Premature Aging Specifically: No	Target Population: Breast cancer survivors
Type of Intervention: Cognitive	
<p>Description of Intervention: Mindfulness-based interventions:</p> <ul style="list-style-type: none"> •Mindfulness-Based Stress Reduction (or MBSR): classes contain elements of controlling and self-regulating attention, in order to help control and reduce stress and associated symptoms. Participants are given education materials on mind-body practices, are instructed to practice meditation at home, and receive practice tools to reduce barriers to mindfulness. •Attention on the breath, focused body-scans, Hatha yoga, and walking meditation are also emphasized as mind-body practices 	
Long Term Cancer Effect Addressed: Cognitive Function	
<p>Summary of Main Points: •Four of the included studies showed beneficial impacts of mindfulness interventions on cognitive function, while two showed no association</p> <ul style="list-style-type: none"> •Mindfulness based interventions show some evidence for improving cognitive impairment among breast cancer survivors 	
<p>Research Gaps: •Studies on mindfulness-based interventions that assess cognition as a primary outcome often do not distinguish between the various domains and focus on only a summary measure of cognitive function, or use measures of self-reported cognitive difficulties, which may indicate other issues of or in addition to cognitive impairment (e.g. depression, personality)</p> <ul style="list-style-type: none"> •Future studies would benefit from more homogeneous outcomes assessments of cognition that are sensitive to the changes reported by cancer patients, particularly using those scales with proven validity and reliability •There is a need for more sensitive measures of cognition that are appropriate to breast cancer survivors, who tend to be non-demented and highly functional. Furthermore, these measures need to be administered in a way that is adequately powered and allows for meta-analysis 	

Ye, M, Du, K, Zhou, J, et al. (2018). A meta-analysis of the efficacy of cognitive behavior therapy on quality of life and psychological health of breast cancer survivors and patients. <i>Psycho-oncology</i> 27: 1695-1703.	
Publication Year: 2018	Type of Review: Meta-analysis
Abstract: OBJECTIVE: The aim of this study was to examine the effect of cognitive behavior therapy (CBT) on quality of life (QOL) and psychological health of breast cancer survivors and patients. METHODS: A total of 1289 references were examined from an overall literature search in PubMed, Embase, CINAHL, and the Cochrane Database of Systematic Reviews. Randomized controlled trials assessing the efficacy of CBT compared with a range of comparators in cancer survivors. We assessed the effect of CBT by using the standardized mean difference as effect size. RESULTS: Among 1289 abstracts and 292 full-text articles reviewed, 10 studies were included. At the posttreatment period, the pooled effect size for CBT on QOL was 0.57 (95% CI, 0.44 to 0.69; P < .001), on depression was -1.11 (95% CI, -1.28 to -0.94; P < .001), on stress was -0.40 (95% CI, -0.53 to -0.26; P < .001), on anxiety was -1.10 (95% CI, -1.27 to -0.93; P < .001), and on hyperarousal cluster of symptoms was -0.18 (95% CI, -0.30 to -0.05; P < .001). The QOL was considered statistically medium effect sizes. The depression and anxiety were considered statistically large effect sizes. CONCLUSIONS: Cognitive behavior therapy is an effective therapy for psychological symptoms of cancer survivors and patients, with meaningfully clinical effect sizes. These findings suggested that CBT should be used as the intervention for breast cancer survivors and patients when possible.	
Addresses Premature Aging Specifically: No	Target Population: Breast cancer survivors and patients
Type of Intervention: Cognitive	
Description of Intervention: Cognitive behavior therapy (CBT)	
Long Term Cancer Effect Addressed: •Psychological health: depression, stress, anxiety •QoL	
Summary of Main Points: Cognitive behavior therapy is an effective therapy for psychological symptoms of cancer survivors and patients, with meaningfully clinical effect sizes (statistically large effect sizes for depression and anxiety) •These findings suggested that CBT should be used as the intervention for breast cancer survivors and patients when possible	
Research Gaps: *Only abstract was reviewed	

Supportive Care Interventions

Original Research

<p>Freeman, LW, White, R, Ratcliff, CG, et al. (2015). A randomized trial comparing live and telemedicine deliveries of an imagery-based behavioral intervention for breast cancer survivors: reducing symptoms and barriers to care. <i>Psycho-oncology</i> 24: 910-918.</p>	
<p>Abstract: OBJECTIVE: This multi-site randomized trial evaluates the quality of life (QOL) benefits of an imagery-based group intervention titled 'Envision the Rhythms of Life'(ERL). METHODS: Breast cancer survivors >6 weeks post-treatment were randomized to attend five weekly 4-h group sessions at a community center with therapist present (live delivery (LD), n = 48), therapist streamed via telemedicine (telemedicine delivery (TD), n = 23), or to a waitlist control (WL) group (n = 47). Weekly individual phone calls to encourage at-home practice began at session one and continued until the 3-month follow-up. Seven self-report measures of QOL were examined at baseline, 1-month and 3-month post-treatments including health-related and breast cancer-specific QOL, fatigue, cognitive function, spirituality, distress, and sleep. RESULTS: The Bonferroni method was used to correct for multiple comparisons, and alpha was adjusted to 0.01. Linear multilevel modeling analyses revealed less fatigue, cognitive dysfunction, and sleep disturbance for LD and TD compared with WL across the follow-up (p's < 0.01). Changes in fatigue, cognitive dysfunction, sleep disturbance, and health-related and breast cancer-related QOL were clinically significant. There were no differences between LD and TD. CONCLUSIONS: Both the live and telemedicine delivered ERL intervention resulted in improvements in multiple QOL domains for breast cancer survivors compared with WL. Further, there were no significant differences between LD and TD, suggesting telemedicine delivered ERL intervention may represent an effective and viable option for cancer survivors in remote areas.</p>	
<p>Publication Year: 2015</p>	<p>Addresses Premature Aging Specifically: No</p>
<p>Target Population: Breast cancer survivors, at least 6 weeks after cancer treatment</p>	<p>Type of Intervention: Supportive Care</p>
<p>Description of Intervention: Psychosocial intervention: Envision the Rhythms of Life (ERL), a telemedicine mind-body intervention delivered to a group: participants were randomized to live delivery group sessions (LD), therapist present via audiovisual technology during group sessions (TD), or waitlist control (WL)</p> <ul style="list-style-type: none"> •Participants had 5 4-hour group sessions at a community center •The sessions included identification of maladaptive passive imagery, active imagery, and practiced targeted imagery •After the 5 sessions, participants had at-home practice (using a 20–30 minute of guided imagery CD) until the 3-month follow-up. Weekly phone calls from therapist to encourage adherence to at-home practice 	
<p>Long Term Cancer Effect Addressed:</p> <ul style="list-style-type: none"> •Cognitive function (perceived) was assessed with the 37-item FACT-Cog •Psychological distress: 18-item Brief Symptom Inventory (BSI-18) Global Severity Index (BSIGSI) •Other outcomes: QoL, sleep disturbances, fatigue 	
<p>Summary of Main Points:</p> <ul style="list-style-type: none"> •The intervention groups, but not the waitlist group, reported a ≥ 10 point improvement in cognitive function and fatigue from baseline to 3-month follow-up •The improvements in cognitive function, fatigue, sleep disturbance, and mental health-related and breast cancer-related QOL were considered clinically significant •The present study provides support for the use of telemedicine delivered at community centers in areas that may not have access to mental healthcare providers 	
<p>Research Gaps:</p> <ul style="list-style-type: none"> •There was low minority representation in the study and future research will examine the efficacy of the ERL program for minority groups •Future studies could document adherence to home practice which was not documented, limiting the ability to examine a “dose effect” of the intervention •Adherence can be documented by providing patients with practice logs or devices (such as MP3 players) equipped to document use of audio files, eliminating the bias inherent in self-reported practice. The lack of an active control group with which to compare the ERL program (versus just usual care) limits the ability to know that the effects are directly attributable to the specific content of the program versus non-specific effects such as social support or attention 	

- A subsequent trial should include an attention control group or other active program for comparison
- Future research is needed to test the long-term benefits of participating in an imagery-based group intervention, after contact with therapists has concluded
- Future research is needed to examine home- or internet-based telemedicine interventions for survivors unable to travel even to community centers
- Future research altering the modules to fit within the schedule of a work-week is warranted

Galantino, ML, Greene, L, Daniels, L, et al. (2012). Longitudinal impact of yoga on chemotherapy-related cognitive impairment and quality of life in women with early stage breast cancer: a case series. Explore (New York, NY) 8: 127-135.

Abstract: PURPOSE: Adjuvant chemotherapy for women with breast cancer has significantly improved the cure rate; however, it has been associated with chemotherapy-related cognitive impact (CRCI). The literature provides preliminary support for the feasibility and efficacy of yoga interventions for the general cancer population, however, controlled trials are scarce and no studies have examined the effect of yoga on cognition for women with breast cancer during chemotherapy. This case series aims to identify the impact of yoga on measures of cognition, functional outcomes, and quality of life (QOL) for breast cancer survivors (BCS). METHODS: Four women with a diagnosis of early-stage breast cancer prior to chemotherapy treatment were administered the following physiologic measures at baseline, 6, and 12 weeks during chemotherapy, and at one and three months after the conclusion of the study: Functional Reach test (balance) and Sit and Reach test (flexibility), and QOL, POMS (Mood) and FACT-B (QOL), at baseline. Primary outcomes of cognition were measured with the Perceived Cognition Questionnaire (PCQ) and CogState, a computerized measurement of cognition. Women attended an Iyengar-inspired yoga program twice a week for 12 weeks. Qualitative questionnaires were administered after the completion of the study to determine perceived benefits and challenges of the yoga program. RESULTS: Four women with Stage II breast cancer ranged in age from 44-65 years. CogState computerized testing showed changes in varying domains of cognition through treatment and follow-up. Improved balance, flexibility, and QOL were also noted over time. No adverse events were observed. Analysis of qualitative data revealed the yoga classes were helpful and subjects continued the practice elements of yoga including relaxation, breathing, and stretching. The most challenging aspect of the study was physical limitations due to various medical complications and included fatigue, decreased range of motion, and pain. CONCLUSION: This case series suggests that yoga may impact various aspects of cognition during and after chemotherapy administration as noted through quantitative measures. Women describe yoga as improving various domains of QOL through the treatment trajectory. This mind-body intervention may stave off CRCI; however, further investigation is needed for additional randomized controlled trials on the effects of yoga on cognition for women with breast cancer undergoing adjuvant chemotherapy treatment.

Publication Year: 2012	Addresses Premature Aging Specifically: No
Target Population: Four women with a diagnosis of early-stage breast cancer going to chemotherapy treatment	Type of Intervention: Supportive Care
Description of Intervention: Yoga: Iyengar-inspired yoga program twice a week for 12 weeks	
Long Term Cancer Effect Addressed: <ul style="list-style-type: none"> •Physical Function: Balance and flexibility tests •Cognitive Function: Perceived Cognition Questionnaire (PCQ) and CogState 	
Summary of Main Points: <ul style="list-style-type: none"> •This case series suggests that yoga may impact various aspects of cognition during and after chemotherapy administration as noted through quantitative measures •Women showed improved balance, flexibility, and QOL after the intervention •Qualitative data revealed the yoga classes were helpful and subjects continued the practice elements of yoga including relaxation, breathing, and stretching 	
Research Gaps: <ul style="list-style-type: none"> •Further investigation is needed for additional randomized controlled trials on the effects of yoga on cognition for women with breast cancer undergoing adjuvant chemotherapy treatment 	

Johns SA, Von Ah D, Brown LF, et al. Randomized controlled pilot trial of mindfulness-based stress reduction for breast and colorectal cancer survivors: effects on cancer-related cognitive impairment. J Cancer Surviv. 2015;10(3):437-48.

Abstract: Purpose—Cancer-related cognitive impairment (CRCI) is a common, fatigue-related symptom that disrupts cancer survivors’ quality of life. Few interventions for CRCI exist. As part of a randomized pilot study targeting cancer-related fatigue, the effects of mindfulness-based stress reduction (MBSR) on survivors’ cognitive outcomes were investigated. Methods—Breast and colorectal cancer survivors (n=71) with moderate-to-severe fatigue were randomized to MBSR (n=35) or a fatigue education and support (ES; n=36) condition. The Attentional Function Index (AFI) and the Stroop test were used to assess survivors’ cognitive function at baseline (T1), after the 8-week intervention period (T2), and 6 months later (T3) using intent-to-treat analysis. Mediation analyses were performed to explore mechanisms of intervention effects on cognitive functioning. Results—MBSR participants reported significantly greater improvement on the AFI total score compared to ES participants at T2 (d=0.83, p=0.001) and T3 (d=0.55, p=0.021). MBSR also significantly outperformed ES on most AFI subscales, although both groups improved over time. MBSR produced greater Stroop accuracy rates relative to ES at T2 (r=0.340, p=0.005) and T3 (r=0.280, p=0.030), with improved accuracy over time only for the MBSR group. There were no significant differences in Stroop reaction time between groups. Improvements in mindfulness mediated the effect of group (e.g., MBSR vs. ES) on AFI total score at T2 and T3. Conclusions—Additional randomized trials with more comprehensive cognitive measures are warranted to definitively assess the efficacy of MBSR for CRCI. Implications for Cancer Survivors—This pilot study has important implications for all cancer survivors as it is the first published trial to show that MBSR offers robust and durable improvements in CRCI.

Publication Year: 2009	Addresses Premature Aging Specifically:
Target Population: Cancer survivors with cancer-related fatigue	Type of Intervention: Supportive Care

Description of Intervention: •**Mindfulness-based stress reduction (MBSR) program compared to fatigue education and support (ES):**

- The MBSR and ES interventions each consisted of 8 weekly 2-h classes led by skilled facilitators
- MBSR training: formal mindfulness meditation practices; didactic instruction (MBSR standard curriculum topics); interactive group discussion of the integration of mindfulness-based self-regulatory skills in daily life
- MBSR facilitators were a physician and a doctoral-level clinical health psychologist with 9 and 3 years of MBSR teaching experience, respectively
- ES sessions: were led by masters-level oncology social workers and included a hybrid of didactic teaching and opportunities to share experiences living with cancer-related symptoms (e.g., fatigue and challenges faced during survivorship such as impact of fatigue on relationships, strategies for symptom self-management such as sleep, eating to maximize energy, increasing physical activity, and survivorship care planning)

Long Term Cancer Effect Addressed: •Cognitive Function: -Subjective measures (The Attentional Function Index); - Objective measures (The Stroop color-word test for executive attentional functioning)

- Mindfulness: The 39-item Five Facet Mindfulness Questionnaire (FFMQ) was used to evaluate the tendency to be mindful in daily life

Summary of Main Points: •MBSR may offer an efficacious and durable means to relieve Cancer-related cognitive impairment (CRCI)

- MBSR participants experienced significant improvement over time on the AFI total score, as well as the Effective Action and Attentional Lapses subscales (significantly exceeding improvements by the ES group)
- The MBSR group’s improvements were durable, lasting at least 6 months after the intervention
- Although their reaction time did not improve relative to ES participants, MBSR participants made significantly fewer errors and their accuracy rate increased over time, whereas the accuracy rate of ES participants did not improve

Research Gaps: •Further research is needed to determine if MBSR has similar benefits for fatigued and non-fatigued survivors with cancer-related cognitive impairment

- The current sample was composed of participants with only two types of cancer, breast and colorectal, which limits generalizability, as does the approximately 50% participation rate

Mao, JJ, Farrar, JT, Bruner, D, et al. (2014). Electroacupuncture for fatigue, sleep, and psychological distress in breast cancer patients with aromatase inhibitor-related arthralgia: a randomized trial. Cancer 120: 3744-3751.

Abstract: BACKGROUND: Although fatigue, sleep disturbance, depression, and anxiety are associated with pain in breast cancer patients, it is unknown whether acupuncture can decrease these comorbid symptoms in cancer patients with pain. The objective of this study was to evaluate the effect of electroacupuncture (EA) on fatigue, sleep, and psychological distress in breast cancer survivors who experience joint pain related to aromatase inhibitors (AIs). METHODS: The authors performed a randomized controlled trial of an 8-week course of EA compared with a waitlist control (WLC) group and a sham acupuncture (SA) group in postmenopausal women with breast cancer who self-reported joint pain attributable to AIs. Fatigue, sleep disturbance, anxiety, and depression were measured using the Brief Fatigue Inventory (BFI), the Pittsburgh Sleep Quality Index (PSQI), and the Hospital Anxiety and Depression Scale (HADS). The effects of EA and SA versus WLC on these outcomes were evaluated using mixed-effects models. RESULTS: Of the 67 randomly assigned patients, baseline pain interference was associated with fatigue (Pearson correlation coefficient [r]=0.75; P < .001), sleep disturbance (r=0.38; P=.0026), and depression (r=0.58; P < .001). Compared with the WLC condition, EA produced significant improvements in fatigue (P=.0095), anxiety (P=.044), and depression (P=.015) and a nonsignificant improvement in sleep disturbance (P=.058) during the 12-week intervention and follow-up period. In contrast, SA did not produce significant reductions in fatigue or anxiety symptoms but did produce a significant improvement in depression compared with the WLC condition (P=.0088). CONCLUSIONS: Compared with usual care, EA produced significant improvements in fatigue, anxiety, and depression; whereas SA improved only depression in women experiencing AI-related arthralgia.

Publication Year: 2014	Addresses Premature Aging Specifically: No
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Target Population: Women with a history of early stage breast cancer (stages I-III) who were currently receiving an aromatase inhibitor (AI), had joint pain for at least three months that they attributed to their AI	Type of Intervention: Supportive Care
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Description of Intervention: Electro-acupuncture (EA) compared to Sham Acupuncture (PLACEBO) and usual care: Two licensed non-physician acupuncturists, administered intervention twice a week for two weeks, then weekly for six more weeks, for a total of ten treatments over eight weeks

- Electro-acupuncture (EA): acupuncturist chose at least four local points around the joint with the most pain and at least four distant points to address non-pain symptoms such as depression/anxiety and fatigue that are commonly seen in conjunction with pain
 - The needles were inserted until “De Qi” (sensation of soreness, tingling, etc.) was reported by the patient.
 - Two pairs of electrodes were connected at the needles adjacent to the painful joint(s) with two hertz electro-stimulation provided by a TENS unit
 - The needles were left in place for 30 minutes with brief manipulation at the beginning and the end of therapy
- Sham Acupuncture (PLACEBO): performed using Streitberger non-penetrating needles at non-acupuncture, non-trigger points at least 5 cm from the joint where pain was perceived to be maximal
 - Instead of adding a small electric current to the needles, the acupuncturists turned on the dial of the TENS unit to a different channel so that the subject could observe the light blinking without receiving the electricity

Long Term Cancer Effect Addressed:

- Pain intensity and interference: measured by the Brief Pain Inventory
- Patient-reported outcomes (PROs) of fatigue, sleep, and psychological distress: measured at Baseline, weeks 2, 4, and 8 during treatment, and at Week 12 (four weeks post-treatment)

Summary of Main Points:

- Electro-acupuncture produced significant and clinically relevant improvement in fatigue, anxiety, and depression as compared to usual care among breast cancer patients who experienced arthralgia related to AI use
- Among breast cancer patients experiencing clinically important joint symptoms attributable to aromatase inhibitors, pain is significantly associated with fatigue, sleep, and depression. Electro-acupuncture shows promise as a therapy to address these symptoms in addition to pain

Research Gaps:

- These preliminary findings need to be confirmed in a larger trial that includes longer follow-up
- Careful incorporation of behavioral instrument and biomarkers in the trial setting can help elucidate the mechanisms underlying both the symptom cluster and the effect of acupuncture

- Given the small group size and the potential concern about multiple comparisons, these results should be interpreted as preliminary. Additional studies will be needed to confirm the efficacy of EA
- Our study also included a 4-week no treatment follow up period, which suggests that the effect of acupuncture for these symptoms persisted, at least for the short term. This is clinically important as continued weekly treatments of acupuncture for a long period of time can be cost-prohibitive and time consuming for most breast cancer patients

Nelson, CJ, Saracino, RM, Roth, AJ, et al. (2019). Cancer and Aging: Reflections for Elders (CARE): a pilot randomized controlled trial of a psychotherapy intervention for older adults with cancer. *Psycho-oncology* 28: 39-47.

Abstract: OBJECTIVE: Cancer and Aging: Reflections for Elders (CARE) is a novel, telephone-delivered intervention designed to alleviate distress in older cancer patients. This pilot randomized controlled trial tested the feasibility and initial efficacy of CARE, drawing from age-appropriate developmental themes and well-established coping theory. METHOD: Eligible patients were ≥ 70 years old; ≥ 6 months post-diagnosis of lung, prostate, breast, lymphoma, or gynecological cancer; on active cancer treatment or within 6 months of ending cancer treatment; and had elevated scores on the Distress Thermometer (≥ 4) or Hospital Anxiety and Depression Scale (≥ 6). Participants completed five sessions of psychotherapy over 7 weeks with assessments at study entry, post-intervention, and 2 months post-intervention. Primary outcomes were feasibility and initial efficacy on anxiety and depression; secondary outcomes included demoralization, coping, loneliness, and spiritual well-being. RESULTS: Fifty-nine participants were randomized to either the CARE arm (n = 31) or the enhanced Social Work Control arm (n = 28). The intervention was feasible and tolerable, meeting a priori criteria for rates of eligibility, acceptance, retention, assessment, and treatment fidelity. Upon completion of the intervention, participants in the CARE arm demonstrated lower mean depression scores (d = 0.58 [CI: 0.04-1.12], P = 0.01) and trended towards increased coping-planning (d = 0.30 [CI: -0.83 to 0.24], P = 0.18). Promising trends in anxiety (d = 0.41 [CI: -0.17 to 0.98], P = 0.10) emerged at 2 months post-intervention; effects for coping-planning dissipated. CONCLUSION: These pilot data suggest the CARE intervention is feasibly delivered, potentially impacts important psychosocial variables, and is accessible for older, frail patients with cancer. Future research will evaluate this intervention on a larger scale.

Publication Year: 2019	Addresses Premature Aging Specifically: Yes
Target Population: Patients ≥ 70 years old; ≥ 6 months post-diagnosis of lung, prostate, breast, lymphoma, or gynecological cancer; on active cancer treatment or within 6 months of ending cancer treatment; and with elevated scores on the Distress or Hospital Anxiety and Dep	Type of Intervention: Supportive Care

Description of Intervention: Psychotherapy (Cancer and Aging: Reflections for Elders (CARE):

- 5 45-minutes sessions over 7 weeks; telephone-facilitated • psychotherapy intervention specifically designed for older cancer patients with the input of older people with cancer
- Draws from age appropriate developmental themes in combination with well-established coping theory to deliver a targeted intervention for older patients in the oncology setting
- It has the potential to be highly accessible to frail older adults who may not be able to attend in-person sessions with regular frequency

Long Term Cancer Effect Addressed:

- Anxiety and depression (higher scores indicating more severe symptoms)
- Demoralization (Demoralization Scale; higher scores indicating worse symptoms)
- Coping
- Loneliness (UCLA Loneliness Scale-Short Form)

Summary of Main Points:

- CARE participants reported reduced depression, anxiety, and demoralization
- These pilot data suggest the CARE intervention is feasibly delivered, potentially impacts important psychosocial variables, and is accessible for older, frail patients with cancer

Research Gaps:

- Future larger trials will include a more racially, ethnically, and educationally diverse sample in order to tailor the CARE intervention as necessary
- Future larger scale studies should make concerted efforts to recruit patients with a range of functional status in order to demonstrate acceptability and outcomes in patients with greater functional impairment
- These preliminary results indicate that the CARE intervention has significant promise and warrants a larger scale RCT
- Further research in a larger study should potentially modify the intervention to include brief monthly booster calls to help maintain the effects of the intervention over time

Wyatt G, Sikorskii A, Rahbar MH, Victorson D, You M. Health-related quality-of-life outcomes: a reflexology trial with patients with advanced-stage breast cancer. *Oncol Nurs Forum.* 2012;39(6):568-77.

Abstract: PURPOSE/OBJECTIVES: To evaluate the safety and efficacy of reflexology, a complementary therapy that applies pressure to specific areas of the feet. DESIGN: Longitudinal, randomized clinical trial. SETTING: Thirteen community-based medical oncology clinics across the midwestern United States. SAMPLE: A convenience sample of 385 predominantly Caucasian women with advanced-stage breast cancer receiving chemotherapy and/or hormonal therapy. METHODS: Following the baseline interview, women were randomized into three primary groups: reflexology (n = 95), lay foot manipulation (LFM) (n = 95), or conventional care (n = 96). Two preliminary reflexology (n = 51) and LFM (n = 48) test groups were used to establish the protocols. Participants were interviewed again postintervention at study weeks 5 and 11. MAIN RESEARCH VARIABLES: Breast cancer-specific health-related quality of life (HRQOL), physical functioning, and symptoms. FINDINGS: No adverse events were reported. A longitudinal comparison revealed significant improvements in physical functioning for the reflexology group compared to the control group (p = 0.04). Severity of dyspnea was reduced in the reflexology group compared to the control group (p < 0.01) and the LFM group (p = 0.02). No differences were found on breast cancer-specific HRQOL, depressive symptomatology, state anxiety, pain, and nausea. CONCLUSIONS: Reflexology may be added to existing evidence-based supportive care to improve HRQOL for patients with advanced-stage breast cancer during chemotherapy and/or hormonal therapy. IMPLICATIONS FOR NURSING: Reflexology can be recommended for safety and usefulness in relieving dyspnea and enhancing functional status among women with advanced-stage breast cancer.

Publication Year: 2012

Addresses Premature Aging Specifically: No

Target Population: 385 predominantly Caucasian women with advanced-stage breast cancer receiving chemotherapy and/or hormonal therapy

Type of Intervention: Supportive Care

Description of Intervention: Reflexology: Defined as a complementary and alternative medicine (CAM) for symptom management or supportive care intervention

- The study comprised three groups: reflexology, lay foot manipulation (LFM), and standard care control
- The intervention comprised four weekly 30-minute sessions of either reflexology or LFM
- Reflexology: stimulation to the nine essential breast cancer-specific reflexes while using reflexology specific deep thumb-walking pressure. With that technique, the reflexologist exerts firm downward pressure with his or her thumb, and then inches forward across the specific reflex
- LFM: The protocol was similar to reflexology, but did not include deep thumb-walking pressure and avoided direct stimulation to the nine breast cancer-specific reflexes

Long Term Cancer Effect Addressed: •Physical Function: SF-36 (overall function) and Functional Assessment of Cancer Therapy-Breast (FACT-B) scale, version 4 for five areas of HRQOL: physical, emotional, social, functional, and other breast cancer-specific concerns

- Pain: Brief Pain Inventory-Short Form
- Depression and anxiety: Center of Epidemiologic Studies-Depression (CES-D) scale and State-Trait Anxiety Inventory
- Fatigue: Center of Epidemiologic Studies-Depression (CES-D) scale

Summary of Main Points: •The current study was the first to have a data and safety monitoring committee, for overseeing reporting of adverse events. Among a vulnerable sample of women with advanced-stage breast cancer, no adverse events were reported

- Reflexology and LFM were safe among even the most fragile patients with advanced-stage breast cancer and contribute to improvements in physical function, dyspnea, and fatigue, but do not affect depressive symptoms, anxiety, pain, and nausea

Research Gaps: •Future studies should seek a more diverse sample

- Reflexology may or may not be readily available in all rural locations; however, many cancer centers where patients seek care have information on local complementary and alternative medicine providers
- Future research could explore cost factors, including the average cost of a reflexology session (\$45 per half hour in many Midwestern locations)
- Research efforts should consider potential physiologic mechanisms of action through biomarkers and the potential for involving lay partners in this therapy for patients with breast cancer as supportive care during chemotherapy

Zick, SM, Sen, A, Hassett, AL, et al. (2018). Impact of self-acupressure on co-occurring symptoms in cancer survivors. JNCI cancer spectrum 2: pky064.	
Abstract: Background: Cancer survivors with fatigue often experience depressive symptoms, anxiety, and pain. Previously, we reported that self-acupressure improved fatigue; however, its impact on other co-occurring symptoms and their involvement in treatment action has not been explored. Methods: Changes in depressive symptoms, anxiety, and pain were examined prior to and following two formulas of self-acupressure and usual care using linear mixed models in 288 women from a previously reported clinical trial. Participants were categorized by random assignment into one of three groups: 1) relaxing acupressure, 2) stimulating acupressure, or 3) usual care. Moderators investigated were body mass index, age, depressive symptoms, anxiety, sleep and pain, and mediators were change in these symptoms. Results: Following treatment, depressive symptoms improved statistically significantly for the relaxing acupressure group (41.5%) compared with stimulating acupressure (25%) and usual care (7.7%). Both acupressure groups were associated with greater improvements in anxiety than usual care, but only relaxing acupressure was associated with greater reductions in pain severity, and only stimulating acupressure was associated with greater reductions in pain interference. There were no statistically significant moderators of sleep quality, anxiety, or depressive symptoms. Fatigue statistically significantly moderated pain, and age statistically significantly modified fatigue. Changes in depressive symptoms and sleep quality statistically significantly mediated the relationship between relaxing acupressure and usual care on fatigue; however, the effect was small. Conclusions: Acupressure was associated with greater improvements than usual care in anxiety, pain, and symptoms of depression in breast cancer survivors with troublesome fatigue. These findings warrant further evaluation in suitably controlled randomized trials.	
Publication Year: 2018	Addresses Premature Aging Specifically: No
Target Population: Females who had stage 0 to III breast cancer, completed primary cancer treatments 12 months or more prior, and were experiencing persistent fatigue	Type of Intervention: Supportive Care
Description of Intervention: Self-acupressure: 10-week, RCT involving two self-administered acupressure protocols, relaxing and stimulating, compared with usual care <ul style="list-style-type: none"> •Acupressure was self-administered daily for 6 weeks followed by a 4-week washout period. Participants had five acupressure visits: screening, baseline, 3 week, 6 week (end of treatment), and 10 week (end of washout phase) 	
Long Term Cancer Effect Addressed: <ul style="list-style-type: none"> •Depressive and anxiety symptoms •Pain •Sleep quality and fatigue 	
Summary of Main Points: <ul style="list-style-type: none"> •Stimulating and relaxing acupressure were associated with greater improvements in anxiety than usual care •Relaxing acupressure was associated with better reductions in depressive symptoms and better decreases in pain severity •Only stimulating acupressure was associated with better decreases in pain interference than usual care 	
Research Gaps: <ul style="list-style-type: none"> •Our investigation into the effects of differing acupressure formulas for co-occurring symptoms in BCS indicates that this intervention may improve symptoms other than fatigue; however, because our findings are only hypothesis-raising, they require confirmation in an independent trial before any clinical recommendations can be made. The underlying mechanisms for these possible effects remain to be elucidated 	

Supportive Care Interventions

Reviews

Buffart, LM, van Uffelen, JG, Riphagen, II, et al. (2012). Physical and psychosocial benefits of yoga in cancer patients and survivors, a systematic review and meta-analysis of randomized controlled trials. BMC cancer 12: 559.	
Publication Year: 2012	Type of Review: Meta-analysis
<p>Abstract: BACKGROUND: This study aimed to systematically review the evidence from randomized controlled trials (RCTs) and to conduct a meta-analysis of the effects of yoga on physical and psychosocial outcomes in cancer patients and survivors. METHODS: A systematic literature search in ten databases was conducted in November 2011. Studies were included if they had an RCT design, focused on cancer patients or survivors, included physical postures in the yoga program, compared yoga with a non-exercise or waitlist control group, and evaluated physical and/or psychosocial outcomes. Two researchers independently rated the quality of the included RCTs, and high quality was defined as >50% of the total possible score. Effect sizes (Cohen's d) were calculated for outcomes studied in more than three studies among patients with breast cancer using means and standard deviations of post-test scores of the intervention and control groups. RESULTS: Sixteen publications of 13 RCTs met the inclusion criteria, of which one included patients with lymphomas and the others focused on patients with breast cancer. The median quality score was 67% (range: 22-89%). The included studies evaluated 23 physical and 20 psychosocial outcomes. Of the outcomes studied in more than three studies among patients with breast cancer, we found large reductions in distress, anxiety, and depression (d = -0.69 to -0.75), moderate reductions in fatigue (d = -0.51), moderate increases in general quality of life, emotional function and social function (d = 0.33 to 0.49), and a small increase in functional well-being (d = 0.31). Effects on physical function and sleep were small and not significant. CONCLUSION: Yoga appeared to be a feasible intervention and beneficial effects on several physical and psychosocial symptoms were reported. In patients with breast cancer, effect size on functional well-being was small, and they were moderate to large for psychosocial outcomes.</p>	
Addresses Premature Aging Specifically: No	Target Population: Adults with any cancer diagnosis either during or post treatment. Included RCT's only had breast cancer and lymphoma patients
Type of Intervention: Supportive Care	
Description of Intervention: Yoga: supervised yoga program with physical poses (yoga asanas), combined with breathing techniques (pranayama) and relaxation or meditation (savasana or dhanya). All yoga classes were led by experienced yoga instructors	
Long Term Cancer Effect Addressed: <ul style="list-style-type: none"> •Physical Outcomes: Physical function •Psychosocial Outcomes: Anxiety, depression, fatigue, distress, sleep, HRQoL 	
Summary of Main Points: <ul style="list-style-type: none"> •Yoga has strong beneficial effects on distress, anxiety and depression •Moderate effects on fatigue, general HRQoL, emotional function and social function •Small effects on functional well-being, and no significant effects on physical function and sleep disturbances 	
Research Gaps: <ul style="list-style-type: none"> •RCTs with larger sample sizes are needed to improve our understanding of the physical and psychosocial effects of yoga •Future studies should also address the optimal duration and frequency of yoga, the effects in patients with types of cancer other than breast cancer, and the optimal time point in the cancer and cancer treatment or rehabilitation trajectories for offering yoga interventions 	

Greenlee, H, Balneaves, LG, Carlson, LE, et al. (2014). Clinical practice guidelines on the use of integrative therapies as supportive care in patients treated for breast cancer. Journal of the National Cancer Institute monographs 2014: 346-358.

Publication Year: 2014	Type of Review: Systematic Review
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Abstract: BACKGROUND: The majority of breast cancer patients use complementary and/or integrative therapies during and beyond cancer treatment to manage symptoms, prevent toxicities, and improve quality of life. Practice guidelines are needed to inform clinicians and patients about safe and effective therapies. METHODS: Following the Institute of Medicine's guideline development process, a systematic review identified randomized controlled trials testing the use of integrative therapies for supportive care in patients receiving breast cancer treatment. Trials were included if the majority of participants had breast cancer and/or breast cancer patient results were reported separately, and outcomes were clinically relevant. Recommendations were organized by outcome and graded based upon a modified version of the US Preventive Services Task Force grading system. RESULTS: The search (January 1, 1990-December 31, 2013) identified 4900 articles, of which 203 were eligible for analysis. Meditation, yoga, and relaxation with imagery are recommended for routine use for common conditions, including anxiety and mood disorders (Grade A). Stress management, yoga, massage, music therapy, energy conservation, and meditation are recommended for stress reduction, anxiety, depression, fatigue, and quality of life (Grade B). Many interventions (n = 32) had weaker evidence of benefit (Grade C). Some interventions (n = 7) were deemed unlikely to provide any benefit (Grade D). Notably, only one intervention, acetyl-L-carnitine for the prevention of taxane-induced neuropathy, was identified as likely harmful (Grade H) as it was found to increase neuropathy. The majority of intervention/modality combinations (n = 138) did not have sufficient evidence to form specific recommendations (Grade I). CONCLUSIONS: Specific integrative therapies can be recommended as evidence-based supportive care options during breast cancer treatment. Most integrative therapies require further investigation via well-designed controlled trials with meaningful outcomes.

Addresses Premature Aging Specifically: No	Target Population: Women receiving standard breast cancer treatment
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Type of Intervention: Supportive Care

Description of Intervention: a.Exercise and awareness interventions: High intensity physical training with relaxation
b.Energy conservation; c. Reflexology; d.Yoga; e.Tai-Chi; f.Multi-Modal - (dance, yoga, meditation, health learning classes); g.Mind-body/Meditation; h.Music therapy; i.Accupuncture; j.Electroacupuncture

Long Term Cancer Effect Addressed: Physical Function; Depression and Mood; Pain

Summary of Main Points: •Physical Function: Sufficient evidence only for Exercise and awareness interventions, evidence against energy conservation, insufficient for the remaining outcomes
•Depression and Mood: Strong evidence for meditation, yoga and relaxation, sufficient for music therapy and acupuncture
•Pain: Moderate evidence of music therapy, a physical training program that includes a mind–body modality and hypnosis, acupuncture, and electroacupuncture

Research Gaps: •A major challenge to interpreting this literature is the lack of standardization of interventions across trials using similar therapeutic approaches (e.g., natural products and mind–body therapies).
•Some integrative therapies are applied in a variety of settings (early vs advanced stages disease, a spectrum of symptom severity), such that the clinical criteria for using some therapies may not be straightforward.
•Many of the approaches identified here are low risk (e.g., stress reduction), and the lack of standardized approaches may not greatly influence their clinical application. Future efforts focusing on increasing levels of reproducibility and standardization should be concentrated on interventions with higher risk profiles

Viscuse, PV, Price, K, Millstine, D, et al. (2017). Integrative medicine in cancer survivors. *Current opinion in oncology* 29: 235-242.

Publication Year: 2017

Type of Review: Narrative Review

Abstract: PURPOSE OF REVIEW: Due to medical advances and an aging population, the number of cancer survivors continues to rise. Survivors often experience late and long-term sequelae of cancer and its treatment (e.g., fatigue, pain, fear of recurrence, and stress). As a result, some patients have utilized or expressed interest in integrative medicine (IM) modalities for prevention of recurrence, optimizing health, enhancing quality of life, and managing symptoms. The purpose of this review is to focus on research published during the past year that informs our understanding of the utility of IM for cancer survivors. RECENT FINDINGS: Physical activity, diet, dietary supplements, mind-body modalities, acupuncture, and massage therapy all may play a role in the management of the physical (e.g., fatigue and pain) and emotional (e.g., anxiety and fear) issues faced by cancer survivors. SUMMARY: IM therapies are appealing to and utilized by many cancer survivors and may reduce symptom burden. Clinicians who provide cancer survivorship care may improve patient care by understanding the evidence for and against their use.

Addresses Premature Aging Specifically: Yes

Target Population: Cancer survivors

Type of Intervention: Supportive Care

Description of Intervention: Integrative medicine: promotes the physical, emotional, and spiritual health of a person by incorporating multiple evidence informed modalities alongside conventional therapy

•The National Center for Complementary and Integrative Health (NCCIH) developed a five domain concept: 1) manipulative & body-based methods, 2) mind-body medicine, 3) alternative medical systems, 4) energy therapies, 5) biologically based therapies

Long Term Cancer Effect Addressed: Long-term sequelae of cancer and its treatment (physical, emotional, mental outcomes)

Summary of Main Points: Recent studies have demonstrated effectiveness of various integrative medicine modalities though there were noted limitations in the methodologies and sample sizes. Such modalities include:

•Physical Activity: Several recent studies have demonstrated the benefit of physical activity for cancer survivors, most notably for quality of life

•Diet: Older epidemiologic studies of diet had identified improved survival after cancer with increased intake of fruits and vegetables, while a whole-food, plant-based diet has been shown to decrease systemic inflammation in newly diagnosed cancer patients. Still, high levels of non-adherence to healthy diet patterns have been found across all ethnic groups in cancer survivors

-Recent studies have examined and demonstrated the feasibility of nutritional interventions with a goal of changing health behavior

•Mind-body modalities (e.g., yoga, qigong, tai chi, meditation, hypnotherapy) have shown beneficial effects in outcomes including, symptom management, QoL, fatigue, pain, stress, anxiety and depression, and cognitive function

•Acupuncture/Acupressure: Preliminary evidence on sleep, fatigue, pain

•Massage: Pooled studies have favored massage therapy for pain, cancer-related fatigue, and anxiety. However, these studies have a high level of heterogeneity, insufficient reporting of data, and inconsistent methodologies (i.e. blinding, allocation concealment), making it challenging to make a strong recommendation for the use of massage therapy in this setting

Research Gaps: •There have been many studies published over the last year that have addressed the feasibility, safety, and efficacy of integrative medicine modalities, including some novel techniques. However, a common theme seems to be the small size and heterogeneous methodologies of many of these studies

•Larger randomized controlled trials are required to definitively identify which integrative medicine techniques are truly beneficial in the setting of cancer survivorship. Such studies should focus on elucidating the optimal candidates and uses for these therapies so they can be most effectively implemented in clinical practice

Winters-Stone, K. (2014). Tai Ji Quan for the aging cancer survivor: mitigating the accelerated development of disability, falls, and cardiovascular disease from cancer treatment. Journal of sport and health science 3: 52-57.	
Publication Year: 2014	Type of Review: Narrative Review
Abstract: Currently there are more than 13.7 million cancer survivors living in the U.S., and that figure is projected to increase by 31% in the next decade, adding another 4 million cancer survivors into the healthcare system. Cancer is largely a disease of aging, and the aging of the population will sharply raise the proportion of older cancer survivors, many of whom will be long-term survivors (5+ years post diagnosis). This review will address the potential utility of exercise to address three health problems that are of particular concern for the aging cancer survivor and the healthcare system, i.e., disability, falls, and cardiovascular disease, because the development of these age-related problems may be accelerated by cancer treatment. While there are many different modes of exercise that each produce specific adaptations, Tai Ji Quan may be a particularly suitable strategy to mitigate the development of age- and cancer-treatment-related problems. Based on studies in older adults without cancer, Tai Ji Quan produces musculoskeletal and cardiometabolic adaptations and is more easily performed by older adults due to its low energy cost and slower movement patterns. Since cancer survivors are mostly older, inactive, and often physically limited by the lingering side effects of treatment, they need to engage in safe, practical, and effective modes of exercise. The dearth of published controlled trials examining the efficacy of Tai Ji Quan to mitigate cancer-treatment-related musculoskeletal and cardiovascular side effects points to ample research opportunities to explore the application of this non-Western exercise modality to improve long-term outcomes for aging cancer survivors.	
Addresses Premature Aging Specifically: Yes	Target Population: Aging cancer survivor
Type of Intervention: Supportive Care	
Description of Intervention: Tai Ji Quan: Series of individual dance-like movements linked in a continuous sequence, flowing slowly and smoothly from one movement to another: <ul style="list-style-type: none"> •It has been used for centuries as a martial arts form •It emphasizes 1) changing the distribution of one's body weight to provide overload sufficient to challenge control of body balance and 2) coordinating breathing and posture changes with mental concentration •The integrated physical and mental effort demanded by Tai Ji Quan distinguishes it from other modes of exercise 	
Long Term Cancer Effect Addressed: Three health problems that are of particular concern for the aging cancer survivor and the healthcare system: <ul style="list-style-type: none"> •Disability (functional limitations, including reduced mobility) •Falls (risk of falls, rates or falls) •Cardiovascular disease (CVD): <ul style="list-style-type: none"> -Cardiotox 	
Summary of Main Points: <ul style="list-style-type: none"> •There are a growing number of studies involving Tai Ji Quan in cancer survivors, but they remain relatively few in number, range vastly in methodologic quality, examine widely differing outcomes (mostly by self-report), and target diverse samples of patients that vary in cancer type and treatments •There are virtually no controlled trials that have examined the potential benefits of Tai Ji Quan on risk factors associated with disability, falls, or CVD in cancer survivors •Some small studies have provided some preliminary evidence on positive impact of Tai Ji on improved aerobic capacity and muscle strength and some beneficial effect on immune function 	
Research Gaps: <ul style="list-style-type: none"> •There is an urgent need to determine whether Tai Ji Quan can reverse or slow the acceleration of aging and onset of side effects associated with cancer treatment, which has implications for reducing clinically meaningful outcomes of disability, falls, and CVD •Only through convincing evidence accumulated from controlled trials with sufficient sample sizes and objectively measured outcomes can it be determined whether engaging in a non-traditional exercise modality, such as Tai Ji Quan, is beneficial for aging cancer survivors, and whether this could lead to more specific and achievable recommendations for cancer survivors for improving motivation •This evidence would strengthen current guidelines and add specificity to recommendations for older cancer Survivors 	

Yang, GS, Kim, HJ, Griffith, KA, et al. (2017). Interventions for the treatment of aromatase inhibitor-associated arthralgia in breast cancer survivors: a systematic review and meta-analysis. Cancer nursing 40: E26-e41.	
Publication Year: 2017	Type of Review: Meta-analysis
<p>Abstract: BACKGROUND: Aromatase inhibitors (AIs) have been established as successful adjuvant therapy for breast cancer survivors. Unfortunately, nearly half of women taking AIs report joint pain, AI-associated arthralgia (AIA). Aromatase inhibitor-associated arthralgia often results in noncompliance, which could lead to cancer recurrence. OBJECTIVE: The purpose of this study was to identify current pain management of AIA and to evaluate the study quality and effects of interventions. METHODS: Nineteen articles published from 2000 to August 2015 were identified using PubMed, CINAHL, PsycINFO, Web of Science, and additional records. Study quality was evaluated by the Quality Assessment Tool for Quantitative Studies. Meta-analysis was used to obtain effect sizes of interventions on pain and subgroups. RESULTS: Five types of interventions emerged: pharmacological approaches, acupuncture, nutritional supplementation, relaxation techniques, and physical exercise. Six studies were strong, 8 were moderate, and 5 were weak in quality. The overall effect size of the interventions on pain was large; pharmacological approaches, acupuncture, and relaxation techniques showed moderate to large effects on pain, whereas nutritional supplementation and physical exercise had no significant effects on it. CONCLUSION: The evidence was based on a body of research with moderate study quality. Although the overall effect of interventions is large, further investigation into the influence of nutrition and physical exercise is needed to better discern their potential for pain management. IMPLICATION FOR PRACTICE: Oncology nurses may be able to implement such validated interventions as pain management modalities to mitigate the symptoms so that breast cancer survivors remain compliant with AIA therapy.</p>	
Addresses Premature Aging Specifically: No	Target Population: Postmenopausal women with a history of stage I, II, or III breast cancer and current use of Aromatase inhibitors (Ais), particularly those who had joint pain associated with AIs
Type of Intervention: Supportive Care	
<p>Description of Intervention: Supportive care intervention to decrease AIA symptoms included:</p> <ul style="list-style-type: none"> •Pharmacological approaches •(Electro)acupuncture •Nutritional supplementation: high dose of vitamin D, glucosamine plus chondroitin, and omega-3 fatty acids •Relaxation techniques: yoga and tai chi •Physical exercise: aerobic and/or resistance exercise 	
Long Term Cancer Effect Addressed: Pain	
<p>Summary of Main Points: •The overall effect size of all interventions on AIA is large and the evidence is based on a body of research with moderate study quality Pharmacological approaches, acupuncture, and relaxation techniques demonstrated a significant effect on pain •Nutritional supplementation and physical exercise do not seem to contribute to control of joint pain</p>	
<p>Research Gaps: •Additional studies with more methodological rigor and diversity may be required to fully evaluate precise effects of nutritional supplementation and physical exercise interventional approaches in AIA's pain •Larger trials to evaluate the therapeutic efficacy of AIA interventions, especially pharmacological approaches and relaxation techniques that have been proven effective in only studies with a small sample size, because large RCT studies may strengthen these bodies of evidence •The use of cost-benefit analysis may potentially play an important role in improving decision-making on which intervention types would be appropriate for further RCTs or developing new interventions by identifying their benefits and deficits</p>	

Other types of interventions

Original Research

<p>Blair, CK, Madan-Swain, A, Locher, JL, et al. (2013). Harvest for health gardening intervention feasibility study in cancer survivors. Acta oncologica (Stockholm, Sweden) 52: 1110-1118.</p>	
<p>Abstract: BACKGROUND: Cancer survivors are at increased risk for second malignancies, cardiovascular disease, diabetes, and functional decline. Evidence suggests that a healthful diet and physical activity may reduce the risk of chronic disease and improve health in this population. METHODS: We conducted a feasibility study to evaluate a vegetable gardening intervention that paired 12 adult and child cancer survivors with Master Gardeners to explore effects on fruit and vegetable intake, physical activity, quality-of-life, and physical function. Throughout the year-long study period, the survivor-Master Gardener dyads worked together to plan/plant three gardens, harvest/rotate plantings, and troubleshoot/correct problems. Data on diet, physical activity, and quality-of-life were collected via surveys; anthropometrics and physical function were objectively measured. Acceptability of the intervention was assessed with a structured debriefing survey. RESULTS: The gardening intervention was feasible (robust enrollment; minimal attrition) and well-received by cancer survivors and Master Gardeners. Improvement in three of four objective measures of strength, agility, and endurance was observed in 90% of survivors, with the following change scores [median (interquartile range)] noted between baseline and one-year follow-up: hand grip test [+ 4.8 (3.0, 6.7) kg], 2.44 meter Get-Up-and-Go [+ 1.0 (+ 1.8, + 0.2) seconds], 30-second chair stand [+ 3.0 (+ 1.0, 5.0) stands], and six-minute walk [+ 11.6 (6.1, 48.8) meters]. Increases of ≥ 1 fruit and vegetable serving/day and ≥ 30 minutes/week of physical activity were observed in 40% and 60%, respectively. CONCLUSION: These preliminary results support the feasibility and acceptability of a mentored gardening intervention and suggest that it may offer a novel and promising strategy to improve fruit and vegetable consumption, physical activity, and physical function in cancer survivors. A larger randomized controlled trial is needed to confirm our results.</p>	
<p>Publication Year: 2013</p>	<p>Addresses Premature Aging Specifically: No</p>
<p>Target Population: 12 cancer survivors of breast, prostate, and childhood cancer (8 adults, 4 parents of 4 child survivors)</p>	<p>Type of Intervention: Other</p>
<p>Description of Intervention: Gardening Intervention: Cancer survivors (and caregivers of child survivors) were paired with Master Gardeners based on geographic location to plan, plant, maintain, and harvest three seasonal gardens at the participants' homes</p> <ul style="list-style-type: none"> •Participants were provided with all necessary equipment and supplies, print materials on garden design, gardening safety and health, and nutrition; however, most gardening knowledge was imparted by working with their assigned Master Gardener •After the initial garden was designed and planted, the Master Gardeners made bimonthly visits to the participants' homes to monitor progress of the garden, assist and provide guidance with any problems •Between visits, communications occurred between dyads via telephone or e-mail to review care of the garden 	
<p>Long Term Cancer Effect Addressed: •Physical Function: 4 objective physical function tests (30-sec chair stand, Get Up & Go Test, six-minute walk test, and grip strength</p> <ul style="list-style-type: none"> •Other outcomes: BMI, fruit and vegetable intake, leisure-time physical activity, HRQoL 	
<p>Summary of Main Points: •The results from this pilot study support the feasibility and acceptability of a mentored vegetable gardening intervention that paired cancer survivors with certified Master Gardeners</p> <ul style="list-style-type: none"> •Results from intervention also provide preliminary support for improvements in fruit and vegetable intake, physical activity levels, and physical functioning •The greatest improvement was observed for physical function. Compared to baseline, one-year follow-up improvement in three of four functional tests was noted in 90% of the cancer survivors 	
<p>Research Gaps: •Randomized controlled trials, larger sample sizes, are needed to evaluate efficacy and durability of vegetable gardening interventions</p>	

Other types of interventions

Reviews

Bradt, J, Dileo, C, Magill, L, et al. (2016). Music interventions for improving psychological and physical outcomes in cancer patients. The Cochrane database of systematic reviews 10.1002/14651858.CD006911.pub3Cd006911

Publication Year: 2016

Type of Review: Systematic Review

Abstract: BACKGROUND: Having cancer may result in extensive emotional, physical and social suffering. Music interventions have been used to alleviate symptoms and treatment side effects in cancer patients. OBJECTIVES: To assess and compare the effects of music therapy and music medicine interventions for psychological and physical outcomes in people with cancer. SEARCH METHODS: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (2016, Issue 1), MEDLINE, Embase, CINAHL, PsycINFO, LILACS, Science Citation Index, CancerLit, CAIRSS, Proquest Digital Dissertations, ClinicalTrials.gov, Current Controlled Trials, the RILM Abstracts of Music Literature, <http://www.wfmt.info/Musictherapyworld/> and the National Research Register. We searched all databases, except for the last two, from their inception to January 2016; the other two are no longer functional, so we searched them until their termination date. We handsearched music therapy journals, reviewed reference lists and contacted experts. There was no language restriction. SELECTION CRITERIA: We included all randomized and quasi-randomized controlled trials of music interventions for improving psychological and physical outcomes in adult and pediatric patients with cancer. We excluded participants undergoing biopsy and aspiration for diagnostic purposes. DATA COLLECTION AND ANALYSIS: Two review authors independently extracted the data and assessed the risk of bias. Where possible, we presented results in meta-analyses using mean differences and standardized mean differences. We used post-test scores. In cases of significant baseline difference, we used change scores. MAIN RESULTS: We identified 22 new trials for inclusion in this update. In total, the evidence of this review rests on 52 trials with a total of 3731 participants. We included music therapy interventions offered by trained music therapists, as well as music medicine interventions, which are defined as listening to pre-recorded music, offered by medical staff. We categorized 23 trials as music therapy trials and 29 as music medicine trials. The results suggest that music interventions may have a beneficial effect on anxiety in people with cancer, with a reported average anxiety reduction of 8.54 units (95% confidence interval (CI) -12.04 to -5.05, $P < 0.0001$) on the Spielberger State Anxiety Inventory - State Anxiety (STAI-S) scale (range 20 to 80) and -0.71 standardized units (13 studies, 1028 participants; 95% CI -0.98 to -0.43, $P < 0.00001$; low quality evidence) on other anxiety scales, a moderate to strong effect. Results also suggested a moderately strong, positive impact on depression (7 studies, 723 participants; standardized mean difference (SMD): -0.40, 95% CI -0.74 to -0.06, $P = 0.02$; very low quality evidence), but because of the very low quality of the evidence for this outcome, this result needs to be interpreted with caution. We found no support for an effect of music interventions on mood or distress. Music interventions may lead to small reductions in heart rate, respiratory rate and blood pressure but do not appear to impact oxygen saturation level. We found a large pain-reducing effect (7 studies, 528 participants; SMD: -0.91, 95% CI -1.46 to -0.36, $P = 0.001$, low quality evidence). In addition, music interventions had a small to moderate treatment effect on fatigue (6 studies, 253 participants; SMD: -0.38, 95% CI -0.72 to -0.04, $P = 0.03$; low quality evidence), but we did not find strong evidence for improvement in physical functioning. The results suggest a large effect of music interventions on patients' quality of life (QoL), but the results were highly inconsistent across studies, and the pooled effect size for the music medicine and music therapy studies was accompanied by a large confidence interval (SMD: 0.98, 95% CI -0.36 to 2.33, $P = 0.15$, low quality evidence). A comparison between music therapy and music medicine interventions suggests a moderate effect of music therapy interventions for patients' quality of life (QoL) (3 studies, 132 participants; SMD: 0.42, 95% CI 0.06 to 0.78, $P = 0.02$; very low quality evidence), but we found no evidence of an effect for music medicine interventions. A comparison between music therapy and music medicine studies was also possible for anxiety, depression and mood, but we found no difference between the two types of interventions for these outcomes. The results of single studies suggest that music listening may reduce the need for anesthetics and analgesics as well as decrease recovery time and duration of hospitalization, but more research is needed for these outcomes. We could not draw any conclusions regarding the effect of music interventions on immunologic functioning, coping, resilience or communication outcomes because either we could not pool the results of the studies that included these outcomes or we could only identify one trial. For spiritual well-being, we found no evidence of an effect in adolescents or young adults, and we

could not draw any conclusions in adults. The majority of studies included in this review update presented a high risk of bias, and therefore the quality of evidence is low. **AUTHORS' CONCLUSIONS:** This systematic review indicates that music interventions may have beneficial effects on anxiety, pain, fatigue and QoL in people with cancer. Furthermore, music may have a small effect on heart rate, respiratory rate and blood pressure. Most trials were at high risk of bias and, therefore, these results need to be interpreted with caution.

Addresses Premature Aging Specifically: No	Target Population: •Participants diagnosed with any type of cancer
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Type of Intervention: Other

Description of Intervention: •**Music therapy interventions:** offered by trained music therapists and involves a therapeutic process and the use of personally tailored music experiences (e.g., use of songs (singing, song writing, and lyric analysis); music improvisation (instrumental and vocal), music and imagery, music-based reminiscence and life review, chanting and toning, music-based relaxation, and instrumental participation)

•**Music medicine interventions:** defined as listening to pre-recorded music for passive listening (e.g., a CD for relaxation or distraction. No systematic therapeutic process is present, nor is there a systematic assessment of the elements and suitability of the music stimulus. Administered by medical or healthcare professionals pre-recorded music

Long Term Cancer Effect Addressed: •Psychological outcomes (e.g. depression, anxiety, anger, hopelessness, helplessness)

•Physical symptoms (e.g., fatigue, nausea, pain)

Summary of Main Points: •Music therapy and music medicine interventions may have a beneficial effect on anxiety in people with cancer (moderate to large effect)

- The results of seven studies suggest that music intervention may reduce depression in people with cancer
- No evidence was found of effect for distress or mood.
- Results of seven trials suggest that music has a large pain-reducing effect. The results of single studies suggest that music listening may reduce the need for anesthetics and analgesics
- Music interventions also had a small to moderate effect on fatigue
- No evidence was found for an effect of music on physical status

Research Gaps: •Future research should explore patient characteristics as moderators of treatment benefits of music therapy interventions versus listening to pre-recorded music

- Future research efforts should aim to enhance understanding of how each of music therapy and music medicine interventions can be optimized for symptom management, how music interventions can best serve patients along the cancer treatment trajectory, and what unique aspects of music therapy and music medicine interventions contribute to the care of patients
- More RCTs are needed to determine the effectiveness of music medicine versus music therapy for outcomes other than quality of life. This can be achieved by including more music medicine as well as music therapy RCTs in future reviews, when these become available or, alternatively, future trials could directly compare the effects of these two types of interventions

Escriva Boulley, G, Leroy, T, Bernetiere, C, et al. (2018). Digital health interventions to help living with cancer: A systematic review of participants' engagement and psychosocial effects. Psycho-oncology 27: 2677-2686.	
Publication Year: 2018	Type of Review: Systematic Review
Abstract: OBJECTIVE: Digital health interventions (DI) open the possibility for cancer patients and survivors to manage the disease and its side effects when they return home after treatment. This study aims to highlight the components of DI, investigate patient engagement with DI, and explore the effects of DI on psychosocial variables. METHODS: In September 2017, we performed a systematic review of studies focusing on DI which target cancer patients or survivors. RESULTS: A total of 29 articles (24 studies) were reviewed. There was considerable heterogeneity in study methods, in outcome definitions, in measures for engagement with DI and in psychosocial variables assessed. Results from the studies showed a high level of engagement. Self-efficacy, psychological symptoms, and quality of life were the most commonly assessed psychosocial variables. However, results for the effect of DI on psychosocial variables were inconsistent. Regarding pain management, results were in line with what one would expect. CONCLUSIONS: The present review showed that despite the heterogeneity in the studies assessed and inconsistent results, DI may constitute an excellent means to help cancer patients and survivors cope better with the disease and with treatment side effects, as they can improve self-management and wellbeing. In order to acquire a greater understanding of the mechanisms underlying cancer patients'/survivors' psychological and behavioral changes in terms of adopting DI, direct comparison between studies is needed. However, this can only come about if methodological and conceptual standardization of DI is implemented.	
Addresses Premature Aging Specifically: No	Target Population: Cancer patients or survivors
Type of Intervention: Other	
Description of Intervention: Digital health interventions (DI): delivered through digital tools including computers, websites, mobile phones, smartphone applications (apps), and wearable devices to foster and support behavioral change	
Long Term Cancer Effect Addressed: <ul style="list-style-type: none"> •Depression and anxiety •Management of symptoms and pain •Quality of life, social support, and weight management or improvement 	
Summary of Main Points: <ul style="list-style-type: none"> •Digital tools used in DI in the cancer context vary depending on the population targeted: <ul style="list-style-type: none"> -Some interventions use cutting-edge wearable DI to promote PA and Wi-Fi weighing scales -The majority used digital tools that already part of most individuals 'everyday lives, (e.g., text messages, computers, smartphones) •Results about DI efficacy in changing psychosocial variables were inconsistent across the studies -Studies mentioning a positive effect of DI highlighted improvement in introjected motivation, and beneficial changes for symptom severity, fear of recurrence, helplessness, fatigue, loss of control over eating, and perceived stress -Depression, stress, and illness intrusiveness were not significantly affected by DI 	
Research Gaps: <ul style="list-style-type: none"> •DI require methodological and conceptual standardizations in order to be able to compare studies and better understand the mechanisms underlying participants' psychological and behavioral changes •DI can assess a wide range of variables in several disciplines which may have different terminology for the same variable. There is a need to agree on a common definition of engagement, and on what psychosocial variables should be assessed and how 	